```
=> d his

     (FILE 'HOME' ENTERED AT 09:59:54 ON 28 NOV 2007)

     FILE 'REGISTRY' ENTERED AT 10:00:02 ON 28 NOV 2007
L1               STRUCTURE UPLOADED
L2             0 S L1

     FILE 'STNGUIDE' ENTERED AT 10:00:46 ON 28 NOV 2007

     FILE 'REGISTRY' ENTERED AT 11:21:30 ON 28 NOV 2007
L3               STRUCTURE UPLOADED
L4            97 S L3 SSS FULL

     FILE 'CAPLUS' ENTERED AT 11:22:03 ON 28 NOV 2007
L5          1188 S L4

     FILE 'STNGUIDE' ENTERED AT 11:22:10 ON 28 NOV 2007

     FILE 'CAPLUS' ENTERED AT 11:23:25 ON 28 NOV 2007
L6            142 S L5 AND PREP/RL
L7             71 S L5 AND (CRYST? OR POLYMORPH? OR XRD? OR X-RAY? OR XRAY OR AMO
L8            186 S L6 OR L7

     FILE 'STNGUIDE' ENTERED AT 11:25:41 ON 28 NOV 2007

     FILE 'REGISTRY' ENTERED AT 11:27:03 ON 28 NOV 2007

=> d l1
L1 HAS NO ANSWERS
L1               STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> d l3
L3 HAS NO ANSWERS
L3               STR
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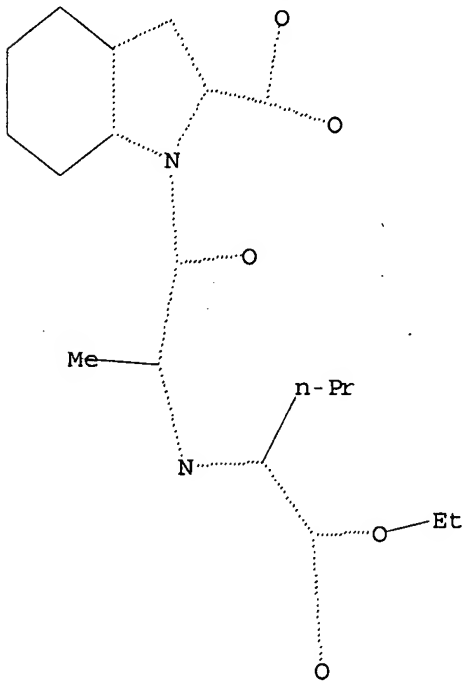


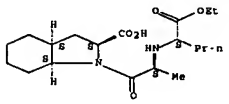
Structure attributes must be viewed using STN Express query preparation.

L8 ANSWER 1 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:1245909 CAPLUS Full-text
TI Test kit for forecasting curative effects of angiotensin-converting enzyme inhibitor
IN Xing, Houxun; Zhang, Yan; Wang, Binyan; Li, Zhiping; Wu, Di; Zang, Tonghua; Xu, Xiping
PA Anhui Institute of Biomedical Sciences, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 23pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 101063166	A	20071031	CN 2006-10011839	20060430
PRAI CN 2006-10011839		20060430		

AB The invention discloses the relationship between single nucleotide polymorphism of prolylcarboxypeptidase (PRCP) E112D site and antihypertensive effects of angiotensin-converting enzyme inhibitor (ACEI). If the genotype is homozygous wild type 112EE, the curative effect of ACEI is good, or else, the curative effects is not obvious. The title test kit comprises polymorphism-typing oligonucleotide for detecting PRCP E112D polymorphism, and related reaction system. The title method is convenient for individual treatment according to individual differences, and can increase curative effects and safety in clinic. The invention can be used for developing anti-hypertension medicines targeting PRCP.
IT INDEXING IN PROGRESS
IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(test kit for forecasting curative effects of angiotensin-converting enzyme inhibitor)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



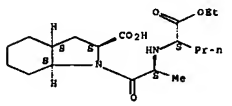
L8 ANSWER 2 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:1245908 CAPLUS Full-text
TI Method for forecasting curative effects of angiotensin-converting enzyme inhibitor
IN Xing, Houxun; Zhang, Yan; Wang, Binyan; Li, Zhiping; Wu, Di; Zang, Tonghua; Xu, Xiping
PA Anhui Institute of Biomedical Sciences, Peop. Rep. China

SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 19pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 101063165	A	20071031	CN 2006-10011836	20060430
PRAI CN 2006-10011836		20060430		

AB The invention discloses the relationship between prolylcarboxypeptidase (PRCP) Glu112Asp (polymorphic site E112D) polymorphism and antihypertensive effects of angiotensin-converting enzyme inhibitor (ACEI, such as benazepril). If the genotype is homozygous wild type 112EE, the curative effect of ACEI is good, or else, the decrease of blood pressure is small. Thus, the polymorphism of PRCP E112D site or the polymorphism of the other PRCP-linked genes can be used for forecasting curative effects of ACEI. The title method is convenient for individual treatment according to individual differences, and can increase curative effects and safety in clinic. The invention can be used for developing anti-hypertension medicines targeting PRCP.
IT INDEXING IN PROGRESS
IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for forecasting curative effects of angiotensin-converting enzyme inhibitor)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 3 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:1237245 CAPLUS Full-text
TI Preparation of 1-heterocyclylamino-2-hydroxy-3-amino-ω-arylalkanes as renin inhibitors for treating hypertension and other renin-mediated diseases
IN Baldwin, John J.; Claremon, David A.; Dillard, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; McGeehan, Gerard; Zeng, Wenguang
PA Vitae Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 89pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2007123718	A1	20071101	WO 2007-US7961	20070330

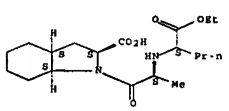
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-787936P P 20060331
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 1-Heterocyclylamino-2-hydroxy-3-amino-ω-arylalkanes of formula I (wherein R1,R3 is H, halogen, cyano, etc.; R2 is H, (C1-C12)alkyl, etc.; R2 and R3 together can also be part of a ring; R4 is H, lower alkyl, hydroxy, etc.; X is methylene or hydroxymethylene; R5 is lower alkyl, lower haloalkyl,etc.; R6 is amino, lower alkylamino, etc.; R7 is H, lower alkyl, etc.; Q is a an oxothiadiazole or a cyclobutenedione; R8 is lower alkyl, lower haloalkyl,etc.)the salts thereof have renin-inhibiting properties and can be used as antihypertensive, medicinally active ingredients. Methods for preparing the compds. are disclosed. Example compound II was prepared by reacting 3,4-dimethoxycyclobut-3-ene-1,2-dione with a methoxybenzyl heptan-3-carbamate to give III, which was subsequently reacted with benzylamine and deprotected. The compds. of the invention exhibited inhibiting activities in in vitro renin inhibition assays at min. concns. of from approx. 5 x 10-5 M to approx. 10-12 M.
IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of 1-heterocyclylamino-2-hydroxy-3-amino-ω-arylalkanes as renin inhibitors for treating hypertension and other diseases)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:1204694 CAPLUS Full-text
DN 147:486433
TI 6-(Aminoalkyl)indazoles as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with renin activity
IN Baldwin, John J.; Claremon, David A.; Dillard, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; McGeehan, Gerard; Zeng, Wenguang
PA Vitae Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 75pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007120523	A2	20071025	WO 2007-US8180	20070330

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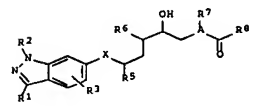
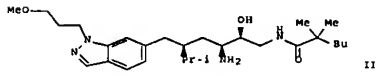
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-788082P P 20060331
GI



I



II

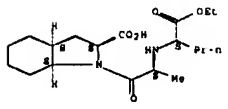
AB 6-(Aminoalkyl)indazoles of formula I and the salts thereof have renin-inhibiting properties and can be used as antihypertensive, and renal, cardiac and vascular protecting medicinally active ingredients. Compds. of formula I

R1 is H, lower (halo)alkyl, (halo)cycloalkyl, amino, CN, etc.; R2 is lower (halo)alkyl, (halo)cycloalkyl, lower (halo)cycloalkylalkyl, lower cyanoalkyl, etc.; R3 is H, CN, and lower (halo)alkyl; X is CH2, CHOH, and lower alkanoyloxymethylene; R5 is lower (halo)alkyl, (halo)cycloalkyl, lower (halo)alkyl-cycloalkyl, etc.; R6 is amino and lower alkylamino; A is N and CH; R7 is H, lower (halo)alkyl, cycloalkyl, and lower (halo)alkoxy-lower alkyl; R8 is lower (halo)alkyl, C8-15 (halo)alkyl, (halo)cycloalkyl, lower alkylcycloalkyl, etc.; and their enantiomers, diastereoisomers and salts thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their renin inhibitory activity (some data given).

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of aminoalkylindazoles as renin inhibitors useful in treatment of diseases - associated with renin activity)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 5 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:1177123 CAPLUS Full-text
DN 147:469237
TI Acylpiperidine compounds as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with aspartic protease activity
IN Baldwin, John J.; Claremon, David A.; Tice, Colin M.; Cacatian, Salvacion; Dillard, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; Mcgeehan, Gerard; Zhao, Wei; Simpson, Robert D.; Singh, Suresh B.; Flaherty, Patrick T.; Kallander, Lara S.; Leach, Colin A.; Lawhorn, Brian; Lu, Qing; Terrell, Lamont R.; Ghavini-Alagha, Bahman; Zhang, Jing; Ghirlanda, Damiano; Hou, Xiaoping; Semus, Simon
PA Vitae Pharmaceuticals, Inc., USA; Smithkline Beecham Corporation
SO PCT Int. Appl., 619pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007117482	A2	20071018	WO 2007-US8339	20070405

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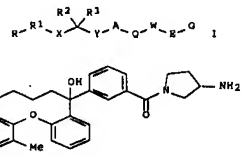
KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-789703P P 20060405
US 2006-789823P P 20060405

GI



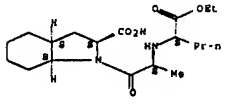
AB Disclosed are compds. according to formula I: wherein the variables are defined herein. Compds. of formula I wherein R is H, C1-8 alkyl, C2-8 alkenyl, C2-8 alkynyl, C3-7 cycloalkyl, C5-7 cycloalkenyl, etc.; R1 is (un)substituted Ph, (un)substituted (mono/bi)cyclic heteroaryl and (un)substituted C3-7 cycloalkyl; X and Y are independently CH2 and a single bond; R2 is H, C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C1-12 alkoxy, etc.; R3 is H, halo, C1-6 alkyl, C1-6 alkoxy, OH, etc.; A is (un)substituted (un)saturated (un)bridge 4- to 7-membered ring; Q and Y are attached to carbon or nitrogen in ring A via 1,2- or 1,3- or 1,4-relationship; Q is CO, CS, SO2, C=CH-NO2, C=N-CN, dioxocyclobutenylene, etc.; W is a bond and (un)substituted C1-5 alkylene; E is (un)substituted (un)saturated (un)bridge 3- to 7-membered ring; G is H, C1-6 alkyl, C4-7 heterocyclyl, OH, NH2 and derivs., etc.; and their enantiomers, diastereoisomers, and pharmaceutically acceptable salts thereof, are claimed. Such compds. are can bind aspartic proteases to inhibit their activity. They are useful in the treatment or amelioration of diseases associated with aspartic protease activity. Also described herein are methods of antagonizing aspartic protease inhibitors in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a compound according to formula I. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their renin inhibitory activity (some data given).

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of acylpiperidine compds. as aspartic protease inhibitors including renin inhibitors useful in treatment of diseases - associated with aspartic protease activity)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 6 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:1177122 CAPLUS Full-text
DN 147:469236
TI Piperidinyl pyrrolidinyl methanone compounds as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with aspartic protease activity
IN Baldwin, John J.; Claremon, David A.; Tice, Colin M.; Cacatian, Salvacion; Dillar, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; Mcgeehan, Gerard; Zhao, Wei; Simpson, Robert D.; Singh, Suresh B.
PA Vitae Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 328pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007117559	A2	20071018	WO 2007-US8520	20070405

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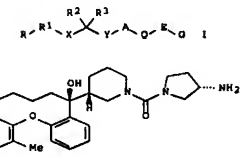
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-789703P P 20060405
US 2006-789823P P 20060405

GI

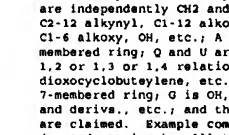


AB Described are compds. of formula I, which are orally active and bind to aspartic proteases to inhibit their activity. They are useful in the treatment or amelioration of diseases associated with aspartic protease activity. Also described are methods of use of the compds. described herein in ameliorating or treating aspartic protease related disorders in a subject in need thereof. Compds. of formula I wherein R is C1-6 alkyl, C2-8 alkenyl, C2-8 alkynyl, C3-7 cycloalkyl, C2-7 cycloalkenyl, etc.; R1 is Ph, (mono/bi)cyclic heteroaryl, benzo-1,3-dioxole, benzo-1,3-dioxin, etc.; X and Y are independently CH2 and a single bond; R2 is H, C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C1-12 alkoxy, C1-12 alkylthio, etc.; R3 is H, halo, C1-6 alkyl, C1-6 alkoxy, OH, etc.; A is (un)substituted (un)saturated (un)bridge 4- to 7-membered ring; Q and U are attached to carbon or nitrogen atoms in ring A in a 1,2 or 1,3 or 1,4 relationship; Q is CO, CS, SO2, C=C-NO2, C=N-CN, dioxocyclobuteylene, etc.; E is (un)substituted (un)saturated (un)bridge 3- to 7-membered ring; G is OH, C1-6 hydroxyalkyl, amino, C1-6 aminoalkyl, C(=NH)NH2 and derivs., etc.; and their enantiomers, diastereoisomers and salts thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their renin inhibitory activity.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of pyrrolidinyl piperidinyl methanone compds. as aspartic protease inhibitors including renin inhibitors useful in treatment of diseases - associated with aspartic protease activity)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



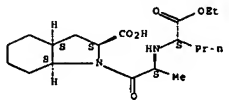
L8 ANSWER 7 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:1175935 CAPLUS Full-text
DN 147:480410
TI Thienopyrimidines having Mnk1/Mnk2 inhibiting activity for pharmaceutical compositions
IN Aicher, Babette; Coulter, Thomas Stephen; Jaekel, Stefan; Kelter, Arndt-Rene; Murfin, Stephen; Reuter, Tanja; Taylor, Steven
PA Develogen Aktiengesellschaft, Germany
SO PCT Int. Appl., 95pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007115822	A1	20071018	WO 2007-EP3186	20070410

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI EP 2006-7454 A 20060407
AB The present invention relates to novel pharmaceutical compns. comprising thienopyrimidine compds. Moreover, the present invention relates to the use of the thienopyrimidine compds. of the invention for the production of pharmaceutical compns. for the prophylaxis and/or treatment of diseases which can be influenced by the inhibition of the kinase activity of Mnk1 and/or Mnk2 (Mnk2a or Mnk2b) and/or variants thereof. The present invention is more particularly directed to the treatment and/or prophylaxis of in particular metabolic diseases of the lipid and carbohydrate metabolism and the consecutive complications and disorders associated therewith.
IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thienopyrimidines having Mnk1/Mnk2 kinase inhibiting activity for pharmaceutical compns. for treating disease and combination with other agents)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:1175900 CAPLUS Full-text
DN 147:469351
TI Piperidines and morpholines as renin inhibitors and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with renin activity
IN Baldwin, John J.; Claremon, David A.; Tice, Colin M.; Cacatian, Salvacion; Dillard, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; Mcgeehan, Gerard; Zhao, Wei; Simpson, Robert D.; Singh, Suresh B.
PA Vitae Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 222pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007117560	A2	20071018	WO 2007-US8521	20070405

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-789723P P 20060405
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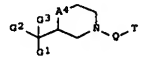

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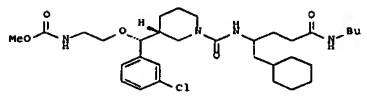
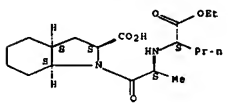


II

AB Described are compds. of formula I which are orally active and bind to renin to inhibit its activity. Compds. of formula I wherein G1 id C1-9 (halo)alkyl, C3-7 (halo)cycloalkyl, C4-9 (halo)cycloalkylalkyl, Ph, etc.; G2 is H, C1-8 (fluoro)alkyl, C4-8 (fluoro)cycloalkylalkyl, C1-8 (fluoro)alkoxy, etc.; G3 is H, halo, OH, C1-4 alkanoylamino, and C1-3 alkoxy; A4 is CH2 and O; Q is CO, CS, SO2, C=C-NO2, C=N-CN, COCO, etc.; T is a mimic of the Leu-Val cleavage site of angiotensinogen; and their enantiomers, diastereoisomers, and salts thereof, are claimed. They are useful in the treatment or amelioration of diseases associated with renin activity. Also described are methods of use of these compds. for treating or ameliorating a renin mediated disorder in a subject. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their renin inhibitory activity.
IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of piperidine and morpholine compds. as renin inhibitors useful in treatment of diseases - associated with aspartic protease and renin activity)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 9 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:971549 CAPLUS Full-text
DN 147:330200
TI Beta crystalline form of the salt of perindopril arginine, its preparation process, and pharmaceutical compositions containing it
IN Coquerel, Gerard; Lefebvre, Loic; Souvie, Jean Claude; Authouart, Pascale
PA Les Laboratoires Servier, Fr.
SO Fr. Demande, 12pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 2897865	A1	20070831	FR 2006-1747	20060228
WO 2007099216	A2	20070907	WO 2007-FR334	20070226
WO 2007099216	A3	20071025		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,

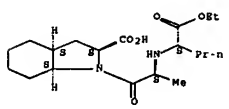
MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI FR 2006-1747 A 20060228
AB Beta crystalline form of arginine salt of perindopril characterized by its X-rays diffraction pattern as a powder is claimed. Arginine salt of perindopril was crystallized from acetonitrile and dried to obtain the beta crystalline form. Formulation of a tablet containing 4 mg of the above salt is disclosed.
IT 612548-45-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(beta crystalline form of salt of perindopril arginine, its preparation process, and pharmaceutical compns. containing it)
RN 612548-45-5 CAPLUS
CN L-Arginine, (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

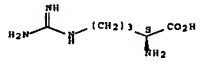
Absolute stereochemistry. Rotation (-).



CM 2

CRN 74-79-3
CMF C6 H14 N4 O2

Absolute stereochemistry.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:971648 CAPLUS Full-text
DN 147:330199
TI Alpha crystalline form of the salt of perindopril arginine, its preparation process, and pharmaceutical compositions containing it
IN Coquerel, Gerard; Lefebvre, Loic; Souvie, Jean Claude; Authouart, Pascale
PA Les Laboratoires Servier, Fr.
SO Fr. Demande, 13pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 2897866	A1	20070831	FR 2006-1748	20060228
WO 2007099217	A1	20070907	WO 2007-FR335	20070226

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI FR 2006-1748 A 20060228

AB Alpha crystalline form of arginine salt of perindopril characterized by its X-rays diffraction pattern as a powder is claimed. Arginine salt of perindopril prepared by the reaction of L-arginine with perindopril. Formulation of a tablet containing 4 mg of the above salt is disclosed.

IT 612548-45-5

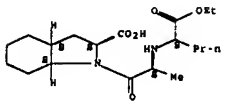
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(alpha crystalline form of salt of perindopril arginine, its preparation process, and pharmaceutical compns. containing it)

RN 612548-45-5 CAPLUS
CN L-Arginine, (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

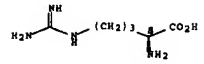
Absolute stereochemistry. Rotation (-).



CM 2

CRN 74-79-3
CMF C6 H14 N4 O2

Absolute stereochemistry.



RE.CNT THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:912792 CAPLUS Full-text
DN 147:243411
TI Pharmaceutical tablets with active and inactive segments
IN Solomon, Lawrence; Kaplan, Allan S.
PA USA
SO U.S. Pat. Appl. Publ., 30pp., Cont.-in-part of U.S. Ser. No. 569,343.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 7

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007190147	A1	20070816	US 2007-693059	20070329
AU 2005245026	A1	20051201	AU 2005-245026	20050523
AU 2005245027	A1	20051201	AU 2005-245027	20050523
AU 2005245028	A1	20051201	AU 2005-245028	20050523
CA 2564960	A1	20051201	CA 2005-2564960	20050523
CA 2564961	A1	20051201	CA 2005-2564961	20050523
CA 2565029	A1	20051201	CA 2005-2565029	20050523
WO 2005112900	A1	20051201	WO 2005-US18631	20050523

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WO 2005112897	A2	20051201	WO 2005-US18633	20050523
WO 2005112897	A3	20060921		

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WO 2005112870	A1	20051201	WO 2005-US18638	20050523

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WO 2005112898	A1	20051201	WO 2005-US18639	20050523

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CA 2566310	A1	20060113	CA 2005-2566310	20050523
AU 2005292670	A1	20060413	AU 2005-292670	20050523
WO 2006038916	A2	20060413	WO 2005-US18632	20050523
WO 2006038916	A3	20061012		

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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 1746979	A2	20070131	EP 2005-825029	20050523

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EP 1750647	A1	20070214	EP 2005-754113	20050523

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EP 1755560	A1	20070228	EP 2005-754171	20050523

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BA, HR, MK, YU

EP 1755564	A2	20070228	EP 2005-754425	20050523

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CN 1960712	A	20070509	CN 2005-80016365	20050523
CN 1964703	A	20070516	CN 2005-80016366	20050523
CN 1993111	A	20070704	CN 2005-80016277	20050523
CN 1997331	A	20070711	CN 2005-80016276	20050523
US 2007031488	A1	20070208	US 2006-441456	20060525
IN 2006KN03322	A	20070615	IN 2006-KN3322	20061113
IN 2006KN03323	A	20070615	IN 2006-KN3323	20061113
IN 2006KN03324	A	20070615	IN 2006-KN3324	20061113
IN 2006KN03325	A	20070615	IN 2006-KN3325	20061113
PRAI US 2004-573042P	P	20040520		
US 2004-573134P	P	20040521		
WO 2005-US18631	W	20050523		
WO 2005-US18632	W	20050523		
WO 2005-US18633	W	20050523		
WO 2005-US18638	W	20050523		
WO 2005-US18639	W	20050523		
US 2006-598267	A2	20060823		
US 2006-598306	A2	20060824		
US 2006-598315	A2	20060824		
US 2006-598344	A2	20060824		
US 2006-569343	A2	20061117		

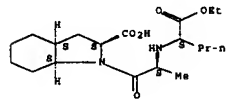
AB An immediate release compressed pharmaceutical tablet that has 2 or more segments and a top and a bottom and has a height that exceeds the width of the tablet. The height is measured vertically from the top to the bottom of the tablet while it is in the tablet die in which it is fully compressed, after compression has been completed. The width is measured as the greatest horizontal dimension of the tablet at a location halfway between the top and the bottom of the tablet, except that when the horizontal cross-section of the tablet is substantially rectangular, the width is defined by locating the two shorter sides of the perimeter of the horizontal cross-section, and measuring the length of a line that is at right angle to the shorter sides.

IT 82834-16-0, Perindopril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical tablets with active and inactive segments)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L6 ANSWER 12 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:912292 CAPLUS Full-text
DN 147:243172

TI Crystalline forms of perindopril erbumine
IN Devarakonda, Surya Narayana; Asnani, Minakshi; Bonnareddy, Sivakumarr Reddy; Padi, Pratap Reddy; Chandramohan, Udhaya Kumar; Chitre, Saurabh Shashikant; Nalivella, Venu; Vasamsetti, Satish Kumar
PA Dr. Reddy's, USA
SO PCT Int. Appl., 27pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

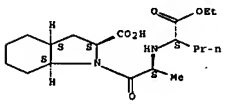
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007092758	A2	20070816	WO 2007-US61524	20070202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI IN 2006-CH177	A	20060203		
US 2006-803087P	P	20060524		
IN 2006-CH970	A	20060606		
US 2006-821178P	P	20060802		
IN 2006-CH1507	A	20060824		
US 2006-868597P	P	20061205		

AB Crystalline forms ζ- and η- of perindopril erbumine are described. Perindopril erbumine was mixed with MeOH for 10 min and the solution was allowed to evaporate slowly to give ζ- form of the compound
IT 107133-36-8, Perindopril erbumine
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystalline forms of perindopril erbumine)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

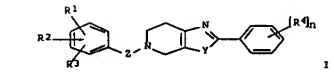


CM 2

CRN 75-64-9
CMF C4 H11 N

L3 ANSWER 13 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:874469 CAPLUS Full-text
DN 147:257759
TI Preparation of substituted thiazolopyridines as PPAR modulators
IN Epple, Robert; Russo, Ross; Azimioara, Mihai
PA IRM LLC, Bermuda
SO PCT Int. Appl., 40pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007089667	A1	20070809	WO 2007-US2316	20070125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2006-763539P	P	20060130		
OS MARPAT 147:257759				
GI				



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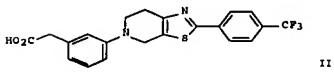
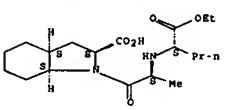


II

AB The title compds. I [n = 0-2; R1 = XCO2R13, OCR11R12XCO2R13 (wherein X = a bond or alkylene; R11, R12 = H, alkyl or alkoxy; or R11 and R12 together with the carbon atom to which R11 and R12 are attached form cycloalkyl; R13 = H, alkyl); R2, R3 = H, halo, alkyl, etc.; Z = a bond, S(O)0-2; Y = O, S; R4 = H, halo, alkyl, etc.], useful as PPAR modulators for treating and preventing PPAR-mediated diseases (no specific data), were prepared Thus, coupling 2-(4-trifluoromethylphenyl)-4,5,6,7-tetrahydro-thiazolo[5,4- c]pyridine with Me (3-bromophenyl)acetate (prepns. given) followed by treating the resulting ester with LiOH afforded 44% II (over 2 steps). The invention relates also to pharmaceutical compns. comprising compds. I and methods of using such compds. to treat or prevent diseases or disorders associated with the activity of the Peroxisome Proliferator- Activated Receptor (PPAR) families.
IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted thiazolopyridines as PPAR modulators useful in treatment and prevention of PPAR-mediated diseases)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

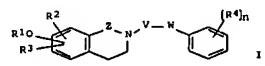


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:873324 CAPLUS Full-text
DN 147:257757
TI Preparation of substituted thiazolyl tetrahydroisoquinolines as PPAR modulators

IN Epple, Robert; Cow, Christopher
PA IRM LLC, Bermuda
SO PCT Int. Appl., 47pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007089557	A2	20070809	WO 2007-US2115	20070125
WO 2007089557	A3	20071108		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, EP, EA, EP, OA				
PRAI US 2006-763623P	P	20060130		
OS MARPAT 147:257757				
GI				



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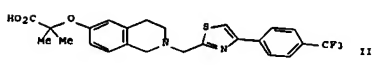


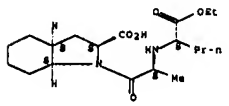
II

AB The title compds. I [n = 0-2; R1 = CR11R12XCO2R13 (wherein X = a bond or alkylene; R11, R12 = H, alkyl, alkoxy; or R11 and R12 together with the carbon atom to which R11 and R12 are attached form cycloalkyl; R13 = H, alkyl); R2, R3 = H, alkyl; V = a bond, alkylene, CONR8, X1C(O)X2 (X1, X2 = a bond, alkylene; R8 = H, alkyl)); W = (un)substituted thiazole, oxazole; Z = CH2, C(O); R4 = H, halo, alkyl, etc.], useful as PPAR modulators for treating and preventing PPAR-mediated diseases (no specific data given), were prepared Thus, reacting Me 2-(1,2,3,4-tetrahydroisoquinolin-6-yloxy)-2-methylpropanoate with 2-(chloromethyl)-4-(4-trifluoromethylphenyl)thiazole followed by treatment of the resulting ester with LiOH and then acidification, afforded the acid II. The invention relates also to pharmaceutical compns. comprising compds. I and methods of using such compds. to treat or prevent diseases or disorders associated with the activity of the Peroxisome Proliferator-Activated Receptor (PPAR) families.
IT 82834-16-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted thiazolyl tetrahydroisoquinolines as PPAR modulators useful in treatment and prevention of PPAR-mediated diseases)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

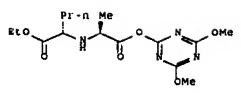


L8 ANSWER 15 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:845244 CAPLUS Full-text
DN 147:212285
TI Process for the preparation of N-[1-(S)-ethoxycarbonyl-1-butyl]-(s)-alanine-DMT complex and its use in the preparation of perindopril
IN Joshi, Narendra Shriram; Pradhan, Nitin Sharad Chandra
PA Glenmark Pharmaceuticals Limited, India
SO PCT Int. Appl., 16pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

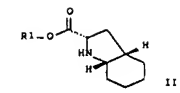
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007086933	A2	20070802	WO 2007-IB150	20070123

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

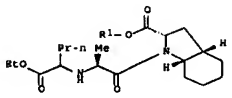
PRAI IN 2006-MU125 A 20060125
US 2006-792875P P 20060418
OS CASREACT 147:212285; MARPAT 147:212285
GI



I



II



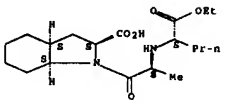
III

AB A process for the preparation of N-[1-(S)-ethoxycarbonyl-1-butyl]-L-alanine-DMT complex (I) by reaction of N-[1-(S)-ethoxycarbonyl-1-butyl]-L-alanine with 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride in a solvent and its use in the synthesis of perindopril, perindopril erbumine or pharmaceutically acceptable salts by reaction of I with compound (II) (R1 = aryl, alkyl, or silyl protective group) in a solvent, following by deprotection of compound (III) using suitable deprotecting agent, is described. Thus, N-[1-(S)-ethoxycarbonyl-1-butyl]-L-alanine and 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride were mixed in THF and stirred for about 10 min at t° = 20-25° under nitrogen. To the resulting solution contained complex I was added (2S, 3aS, 7aS)-benzyl-perhydroindole-2-carboxylate at t° = 20-25° under nitrogen, and after separation and purification 1.5 g of perindopril benzyl ester was obtained, which was transformed into perindopril tert-Bu amine salt.

IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ethoxycarbonylbutyl alanine DMT complex and its use in preparation of perindopril and perindopril erbumine)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



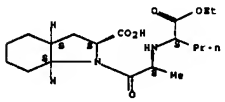
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



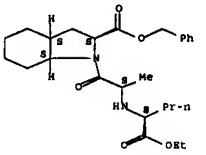
CM 2

CRN 75-64-9
CMF C4 H11 N

IT 122454-52-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of ethoxycarbonylbutyl alanine DMT complex and its use in preparation of perindopril and perindopril erbumine)

RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



L1 ANSWER 16 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:845231 CAPLUS Full-text
DN 147:235167
TI Spiro imidazole derivatives as PPAR modulators and their preparation, pharmaceutical compositions and use in the treatment of diseases associated with PPAR activity.
IN Epple, Robert; Russo, Ross; Azimioara, Mihai; Cow, Christopher; Molteni, Valentina; Li, Xiaolin; Chianelli, Donatella
PA IRM LLC, Bermuda
SO PCT Int. Appl., 101pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007087448	A1	20070802	WO 2007-US2315	20070125

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2006-763557P P 20060130
OS MARPAT 147:235167
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides compds. I and II, pharmaceutical compns. comprising such compds. and methods of using such compds. to treat or prevent diseases or disorders associated with the activity of the Peroxisome Proliferator-Activated Receptor (PPAR) families. Compds. of formula I and II wherein A is (un)substituted Ph and (un)substituted thiazol-2-yl; n and m are independently 1 - 5; each R1 is independently H, halo, C1-6 (halo)alkyl, and C1-6

(halo)alkoxy; R3 is C1-8 alkyl, C2-8 alkenyl, C1-6 haloalkyl, C2-6 haloalkenyl, etc.; R4 and R5 are independently H and C1-6 alkyl; or R4R5 taken together to form =O; Y is N and CH; Z is a bond, SO0-2, CH2, etc.; A and B are independently CH and N; R6 and R7 are independently H, halo, C1-6 (halo)alkyl and C1-6 (halo)alkoxy; R8 is CO2H and derivs., C1-4 alkylene-CO2H and derivs., etc.; R9 and R10 are independently H, C1-6 alkyl, and OH and derivs.; and their pharmaceutically acceptable salts, hydrates, solvates, isomers and prodrugs thereof, are claimed. Example compound III was prepared by N-alkylation of 3-isobutyl-1-[2-(4-methoxyphenyl)ethyl]-1,3,8-triazaspiro[4,5]decane-2,4-dione with Et 3-bromomethylphenylacetate followed by hydrolysis. All the invention compds. were evaluated for their PPAR modulatory activity (some data given).

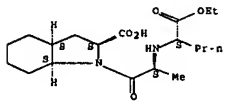
IT 107133-36-8, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of spiro imidazole derivs. as PPAR receptor modulators useful in treatment and prevention of diseases - associated with PPAR receptors activity)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:675141 CAPLUS Full-text
DN 147:79625
TI Association of a sinus node If current inhibitor, ivabradine, with an angiotensin converting enzyme inhibitor, and pharmaceutical compositions containing it for treating arterial hypertension
IN Benatar, Vidal; Lerebours-Pigeonniere, Guy
PA Les Laboratoires Servier, Fr.
SO U.S. Pat. Appl. Publ., 6pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2007142355	A1	20070621	US 2006-642899	20061220
	FR 2894825	A1	20070622	FR 2005-13006	20051221
	SG 133545	A1	20070730	SG 2006-8805	20061218
	NO 2006005905	A	20070622	NO 2006-5905	20061219
	IN 2006DE02713	A	20070803	IN 2006-DE2713	20061219
	EP 1800678	A1	20070627	EP 2006-291993	20061220
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	WO 2007077327	A1	20070712	WO 2006-FR2803	20061220
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	CA 2571644	A1	20070621	CA 2006-2571644	20061221
	KR 2007066921	A	20070627	KR 2006-131721	20061221
	AU 2006252210	A1	20070705	AU 2006-252210	20061221
	JP 2007169283	A	20070705	JP 2006-343823	20061221
	CN 101015557	A	20070815	CN 2006-10064318	20061221
	BR 2006005517	A	20071016	BR 2006-5517	20061221
PRAI	FR 2005-13006	A	20051221		

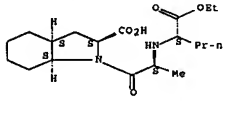
AB The present invention relates to a new association comprising a selective and specific sinus node If current inhibitor, more especially ivabradine, and an agent that inhibits angiotensin-converting enzyme. Angiotensin-converting enzyme inhibitors are one of the major therapeutic classes in the treatment of arterial hypertension. It has been now discovered that selective and specific sinus node If current inhibitors, more especially ivabradine, are capable of potentiating the effects of agents that inhibit angiotensin-converting enzyme. The invention relates more especially to the association between ivabradine, or one of its hydrates, crystalline forms and addition salts with a pharmaceutically acceptable acid, more especially its hydrochloride, and perindopril, or one of its hydrates, crystalline forms and addition salts with a pharmaceutically acceptable base, more especially its arginine or tert-butylamine salt. Medicinal products containing such association which are useful in treating arterial hypertension are described. Thus, pharmaceutical composition of antihypertensive tablets was formulated comprising 7.5 mg ivabradine hydrochloride, 2 mg perindopril tert-butylamine, 62 mg lactose

monohydrate, 1.3 mg magnesium stearate, 9 mg povidone, 0.3 mg anhydrous colloidal silica, 30 mg cellulose sodium glycolate, and 2.6 mg stearic acid. A great reduction in systolic and diastolic arterial pressure was observed in clin. studies with hypertensive patients.

IT 82834-16-0, Perindopril 107133-36-8 612548-45-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sinus node current inhibitor ivabradine association with an angiotensin converting enzyme inhibitor and pharmaceutical compns. containing it for treating arterial hypertension)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

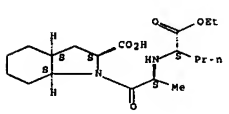


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

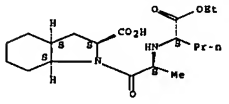
CRN 75-64-9
CMF C4 H11 N

RN 612548-45-5 CAPLUS
CN L-Arginine, (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

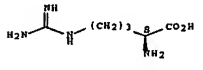
Absolute stereochemistry. Rotation (-).



CM 2

CRN 74-79-3
CMF C6 H14 N4 O2

Absolute stereochemistry.



L8 ANSWER 18 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:647580 CAPLUS Full-text
DN 147:88914
TI Use of methylenetetrahydrofolate reductase gene polymorphisms in predicting homocysteine level, homocysteine-associated disease risks, and angiotensin converting enzyme inhibitor-related drug treatment responses in humans
IN Xu, Xiping; Fang, Zhian; Jiang, Shanqun; Wang, Binyan; Yang, Jianhua; Zhang, Shanchun; Mao, Guangyun; Xing, Houxun; Liu, Ping; Wang, Yan; Zang, Tonghua; Wang, Mengde; Wang, Yu; Dai, Chengxiang; Zhang, Kerong
PA USA
SO U.S. Pat. Appl. Publ., 32pp.

CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

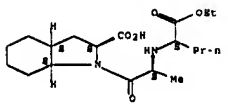
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007134709	A1	20070614	US 2006-638634	20061213
CN 1982471	A	20070620	CN 2005-10130528	20051214
CN 101037708	A	20070919	CN 2006-10064915	20060317
PRAI CN 2005-10130528	A	20051214		
CN 2006-10064915	A	20060317		
CN 2006-10090093	A	20060627		

AB This invention features our discovery on usages of methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms in predicting homocysteine (Hcy) level and/or incidence and prognosis of diseases associated with increased Hcy level in a subject, as well as predicting treatment effects of medicines in the category of Angiotensin converting enzyme inhibitor (ACEI) with and without combination with B Vitamins. Polymorphisms within gene MTHFR that are analysed in this invention include nucleotides C677T, A1298C, G1793A, G215A, G482A, and A1317G. This invention also features our discovery on laboratory and anal. methods that are essential to the above described usages of MTHFR gene polymorphisms. In addition, this invention features a kit that has translated the above discoveries into a practical and reliable tool that can be applied to accomplish the above described usages of MTHFR gene polymorphisms. This invention represents an important step in realizing personalized medicine, with the goal to tailor diagnosis, prevention and treatment strategy to meet individual needs.

IT 82834-16-0, Perindopril
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(use of human gene MTHFR polymorphisms in predicting homocysteine level, homocysteine-associated disease risks, and ACEI-related treatment responses)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LS ANSWER 19 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:619669 CAPLUS Full-text
DN 147:30943
TI Process for the preparation of perindopril using purified N-[(S)-1-carbethoxybutyl]-(S)-alanine and/or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid or activated or protected forms thereof.
IN Chen, Weiren; Shi, Jiaxiang; Lu, Biao

PA Krka, Tovarna Zdravil, D.D., Novo Mesto, Slovenia
SO PCT Int. Appl., 27pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

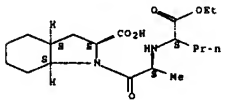
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007062865	A1	20070607	WO 2006-EP11558	20061201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1792896	A1	20070606	EP 2005-26160	20051201
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
PRAI EP 2005-26160	A	20051201		
SI 2004-143	A	20040514		

AB A process for the preparation of (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid uses purified intermediates N-[(S)-1-carbethoxybutyl]-(S)-alanine and/or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid or activated or protected forms thereof, wherein the purified form has been prepared using THF, di-Me carbonate, di-Et carbonate, 1,2-dimethoxyethane, tert-Bu Me ether, 2-methyltetrahydrofuran, cyclopentyl Me ether, or mixts. thereof.

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril using purified carbethoxybutylalanine and/or octahydroindolecarboxylic acid or activated or protected forms thereof)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



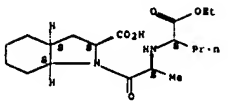
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

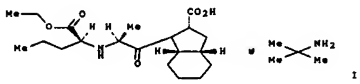
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 20 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:563460 CAPLUS Full-text
DN 146:528317
TI Preparation of stable formulation of amorphous perindopril salts and their use in the therapy of hypertension
IN Rucman, Rudolf; Zupet, Pavel
PA Diagen Smartno Pri Ljubljani, D.O.O., Slovenia
SO PCT Int. Appl., 34pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007058634	A1	20070524	WO 2006-SI34	20061108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK,				

MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRAI SI 2005-314 A 20051117
SI 2006-177 A 20060731

GI



I

AB There is disclosed a stable formulation of amorphous perindopril erbumine (I) which is obtained in such a way that I, which may also be prepared in situ from perindopril and tert-butylamine, or I hydrate is dissolved in demineralized water or in a mixture of demineralized water and alc., to this solution a solution of sodium hydrogen carbonate is added for stabilization, inert ingredients for tabletting are wetted therewith, dried in vacuo by lyophilization or at normal pressure with a stream of warm air at not more than 40°, hydrophobic additives to facilitate tabletting are added, it is homogenized and the granulate is tabletted. Disclosed is also a stable formulation of amorphous perindopril sodium salt obtained by modification of the drying procedure in the process of preparing the granulate. X-ray powder diffraction investigations show that I is present in amorphous form and does not contain crystal α, β and γ forms.

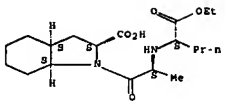
IT 107133-36-8P, Perindopril erbumine 690267-97-2P
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of stable formulation of amorphous perindopril salts and their use in therapy of hypertension)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

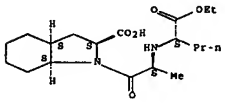
CRN 75-64-9
CMF C4 H11 N

RN 690267-97-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

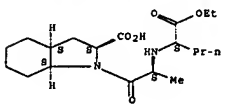


CM 2

CRN 75-64-9
CMF C4 H11 N

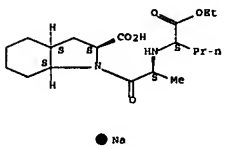
IT 82834-16-0, Perindopril
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(preparation of stable formulation of amorphous perindopril salts and their use in therapy of hypertension)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 869954-09-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of stable formulation of amorphous perindopril salts and their use in therapy of hypertension)
RN 869954-09-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, sodium salt (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:538695 CAPLUS Full-text
DN 146:521789
TI Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Cow, Christopher; Azimioara, Mihai; Russo, Ross; Xie, Yongping; Wang, Xing
PA IRM LLC, Bermuda
SO PCT Int. Appl., 139pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007056366	A2	20070518	WO 2006-US43342	20061107
WO 2007056366	A3	20070705		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

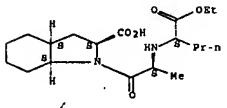
PRAI US 2005-734683P P 20051107
OS MARPAT 146:521789
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazoles and thiazoles of formula I, which modulate the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPARδ. In compds. I, W is O or S; R1 is -L1-X-C(R7R8)-L2-CO2R9; L1 and L2 are independently a bond or C1-4 alkylene; X is a bond, O, or S; R7 and R8 are independently H, C1-4 alkyl, or C1-4 alkoxy; R9 is H or C1-6 alkyl; p is 0-3; each R2 is independently selected from halo, C1-6 alkyl, C2-6 alkenyl, C1-4 alkoxy, C1-4 alkylthio, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; n is 0-3; R3 and R4 are independently H or C1-6 alkyl; R5 and R6 are independently selected from H, C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl; Y is O, S, NR10, or CR10R11; Z is C10R11 or S; and R10 and R11 are independently selected from H and C1-6 alkyl; including salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I with one or more pharmaceutically acceptable excipients, optionally containing another active ingredient selected from antidiabetic agents, hypolipidemic agents, antiobesity agents, antihypertensive agents, etc., as well as to the use of the compns. for the

treatment or prevention of disease or disorders associated with PPAR activity. Regioselective acetylation of Et (2-methylphenoxy)acetate followed by Baeyer-Villiger oxidation, methanolysis, and regioselective bromination gave phenoxyacetate II, which underwent O-silylation, Suzuki coupling with cyclopropylboronic acid, and desilylation resulting in the formation of cyclopropylphenoxyacetate III. Substitution of 3-chloropropanol with potassium cyanide followed by sulfolysis to the thioamide and heterocyclization with 2-bromo-1-(4-trifluoromethylphenyl)ethanone formed thiazole IV, which was coupled to III under Mitsunobu conditions and hydrolyzed to give thiazole V. The compds. of the invention, e.g., V, are modulators of PPAR, particularly PPARδ (no data).
IT 82834-16-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of oxazole and thiazole compds. as PPAR modulators)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L9 ANSWER 22 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:538194 CAPLUS Full-text
DN 146:521786
TI Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Cow, Christopher; Azimioara, Mihai; Russo, Ross
PA IRM LLC, Bermuda
SO PCT Int. Appl., 62pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007056496	A1	20070518	WO 2006-US43586	20061107

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-734678P P 20051107

OS MARPAT 146:521786

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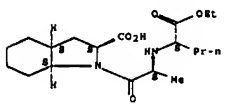


* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazoles and thiazoles of formula I, which modulate the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPARδ. In compds. I, W is O or S; R1 is -L1-X-C(R6R9)-L2-CO2R10; L1 and L2 are independently a bond or C1-4 alkylene; X is a bond, O, or S; R8 and R9 are independently H, C1-4 alkyl, or C1-4 alkoxy; R10 is H or C1-6 alkyl; p is 0-3; each R2 is independently selected from halo, C1-6 alkyl, C2-6 alkenyl, C1-4 alkoxy, C1-4 alkylthio, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; n is 0-3; R3 and R4 are independently H or C1-6 alkyl; R5 and R6 are independently selected from H, C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl; R7 is H, C1-6 alkyl, -L3-C6-12 aryl, -L3-C3-12 cycloalkyl, -L3-OR11, or -L3-N(R11R12); L3 is a bond or C1-4 alkylene; and R11 and R12 are independently H or C1-6 alkyl; including salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I with one or more pharmaceutically acceptable excipients, optionally containing another active ingredient selected from anti-diabetic agents, hypolipidemic agents, anti-obesity agents, anti-hypertensive agents, etc., as well as to the use of the compns. for the treatment or prevention of disease or disorders associated with PPAR activity. Regioselective bromination of 4-benzyloxyphenol followed by O-silylation, substitution with tetramethyltin, and desilylation gave 4-benzyloxy-2-methylphenol, which underwent substitution of Me 2-bromo-2-methylpropionate, debenzylation, and substitution of 1,2-dibromoethane resulting in the formation of ester II. Heterocyclization of 2-bromo-1-(4-trifluoromethylphenyl)ethanone with thiourea formed aminothiazole III, which underwent substitution of bromide II, N-methylation, and ester hydrolysis to give thiazole IV. The compds. of the invention, e.g., IV, are modulators of PPAR, particularly PPARδ (no data).

IT 82834-16-0, Perindopril

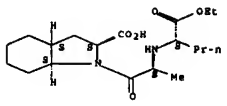
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(codrug; preparation of oxazole and thiazole compds. as PPAR modulators)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:536876 CAPLUS Full-text

DN 146:521785

TI Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy

IN Epple, Robert; Xie, Yongping; Wang, Xing; Russo, Ross; Cow, Christopher; Azimioara, Mihai

PA IRM LLC, Bermuda

SO PCT Int. Appl., 80pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007056497	A1	20070518	WO 2006-US43587	20061107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2005-734592P	P	20051107		

OS MARPAT 146:521785

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazoles and thiazoles of formula I, which modulate the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPARδ. In compds. I, W is N or CH; Y is O, S, CH2CH2, or CR5R6, where R5 and R6 are independently selected from H and C1-6 alkyl; Z is S or O; R1 is -L1-X-C(R7R8)-L2-CO2R9; L1 and L2 are independently a bond or C1-4 alkylene; X is a bond, O, or S; R7 and R8 are independently H, C1-4 alkyl, or C1-4 alkoxy, or R7 and R8, together with the carbon atom to which they are attached, form C3-12 cycloalkyl; R9 is H or C1-6

alkyl; n is 0-3; each R2 is independently selected from halo, C1-4 alkyl, C1-4 alkoxy, C1-4 alkylthio, and C3-12 cycloalkyl; R3 is C1-8 alkyl; and R4 is selected from halo, C1-4 alkyl, C1-4 haloalkyl, and C1-4 haloalkoxy; including salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I with one or more pharmaceutically acceptable excipients, optionally containing another active ingredient selected from anti-diabetic agents, hypolipidemic agents, anti-obesity agents, anti-hypertensive agents, etc., as well as to the use of the compns. for the treatment or prevention of disease or disorders associated with PPAR activity. Diazotization of 4- (trifluoromethoxy)acetophenone followed by heterocyclization with acetonitrile, and sequential double bromination gave dibromooxazole II. O-Benzylation of 4-hydroxybenzaldehyde, condensation with Et ethoxyacetate, and hydrogenation resulted in the formation of ethoxypropionate III, which underwent substitution of II followed by Suzuki coupling with 2-isopropoxy-5-pyrimidineboronic acid (two-step preparation from 5-bromo-2-chloropyrimidine is given) and ester hydrolysis to give oxazole IV. The compds. of the invention, e.g., IV, are modulators of PPAR, particularly PPARδ (no data).

IT 82834-16-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(codrug; preparation of oxazole and thiazole compds. as PPAR modulators)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:465597 CAPLUS Full-text

DN 146:482092

TI Combination of a dipeptidyl peptidase-4 inhibitor and an anti-hypertensive agent for the treatment of diabetes and hypertension

IN Hasegawa, Philip A.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 42pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007050485	A2	20070503	WO 2006-US41233	20061020

WO 2007050485	A3	20070927	
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
PRAI US 2005-730167P	P	20051025	

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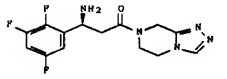


I

AB The invention relates to pharmaceutical compns. comprising a combination of a particular dipeptidyl peptidase-4 (DPP-4) inhibitor I and an anti-hypertensive agent selected from the group consisting of an angiotensin II receptor antagonist and an angiotensin converting enzyme inhibitor, kits containing such combinations and methods of using such compns. for the treatment of diabetes, diabetes-related disorders, hypertension, and hypertension-related disorders. Example compound I and I•H3PO4 was prepared by a multistep procedure (procedure given). Compound I and I•H3PO4 were evaluated for their DPP-4 inhibitory activity.

IT 82834-16-0, Perindopril

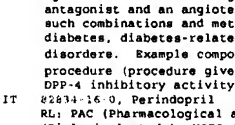
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of sitagliptin phosphate and combination of particular DPP-4 inhibitor and antihypertensive agent selected from angiotensin II receptor antagonist and ACE inhibitor for treatment of diabetes and hypertension)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 25 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:201253 CAPLUS Full-text
DN 146:259149
TI New crystalline form of perindopril erbumine
IN Griesser, Ulrich; Niederwanger, Verena
PA Sandoz A.-G., Switz.
SO PCT Int. Appl., 21pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007020009	A1	20070222	WO 2006-EP7923	20060810

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI SI 2005-231 A 20050812

AB The present invention relates to new crystalline form of the ACE inhibitor perindopril and processes for the preparation thereof. Cryst . form D of perindopril erbumine is formulated into a pharmaceutically acceptable dosage form, such as a tablet, pill, capsule or injectable for use in the treatment of cardiovascular diseases. Thus, 0.25 g of perindopril erbumine form α were suspended in 5 mL of dichloromethane and the suspension was heated up to 40°. The clear solution was cooled down to room-temperature at a rate of about 10K/h, filtered under reduced pressure and air-dried to yield 0.23 g (92%) perindopril erbumine crystalline form D.

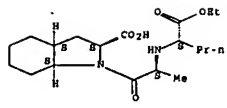
IT 107133-36-8, Perindopril erbumine
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of crystalline form of perindopril erbumine for dosage forms)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:200622 CAPLUS Full-text
DN 146:259148
TI A process for the preparation of perindopril erbumine for dosage forms
IN Ham, Zoran; Furlan, Borut
PA Lek Pharmaceuticals D.D., Slovenia
SO PCT Int. Appl., 26pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007020012	A1	20070222	WO 2006-EP7926	20060810

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI SI 2005-232 A 20050812

AB The present invention relates to a new process for the preparation of pure perindopril erbumine. The present invention also relates to a new process for the preparation of crystalline form D of perindopril erbumine. Crystalline

perindopril erbumine is formulated into a pharmaceutically acceptable dosage form. Thus, (2S,3aS,7aS)-2-carboxyperhydroindole benzyl ester was treated with N-((S)-1-carbetoxybutyl)-(S)-alanine in acetonitrile in presence of O-(benzotriazol-1-yl)-N,N,N',N'- tetramethyluronium hexafluorophosphate to afford 88% perindopril benzyl ester. Hydrogenolysis of crude perindopril benzyl ester over 10% Pd/C gave crude perindopril (2.33% of diketopiperazine I, 0.54% of diketopiperazine II). Crude perindopril was dissolved in wet Et acetate, insol. impurities were filtered off, tert-butylamine was added to the filtrate, the mixture was heated to boiling, filtered and then cooled to 0° to precipitate perindopril erbumine in crystalline form D.

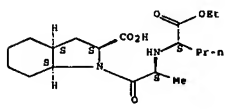
IT 107133-36-8P, Perindopril erbumine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of perindopril erbumine and its crystalline form for dosage forms)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

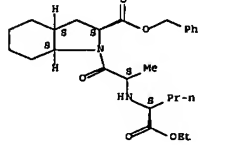
CRN 75-64-9
CMF C4 H11 N

IT 82834-16-0P, Perindopril 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril erbumine and its crystalline form for dosage forms)

RN 82834-16-0 CAPLUS

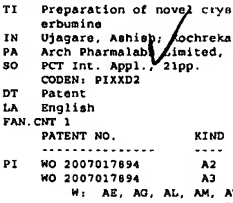
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:175534 CAPLUS Full-text
DN 146:236294
TI Preparation of novel crystalline η (eta) form of perindopril erbumine
IN Ujagare, Ashish; Kochrekar, D. A.; Sarjekar, Pushpalata
PA Arch Pharmalabs Limited, India
SO PCT Int. Appl., 21pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007017894	A2	20070215	WO 2006-IN156	20060504
WO 2007017894	A3	20070510		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI IN 2005-MU561 A 20050505

AB The present invention relates to a novel crystalline η form of perindopril erbumine exhibiting characteristic 2θ values and having purity not less than 99.8%. More particularly, the present invention relates to a process for the preparation of the novel crystalline η form of perindopril erbumine comprising the steps of (i) dissolving perindopril erbumine monohydrate in halogenated hydrocarbon solvent; (ii) adding a co-solvent to the mixture of the content obtained from step (i); (iii) removing the mixture of solvents under reduced pressure in the range of 25 to 35°; and (iv) filtering off the solid obtained.

IT 107133-36-8P, Perindopril erbumine
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation and purification of η crystal form of perindopril erbumine of high purity and good solubility)

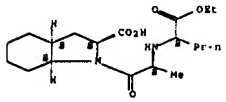
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

IT 690267-97-1P, Perindopril erbumine monohydrate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation and purification of η crystal form of perindopril erbumine of high purity and good solubility)

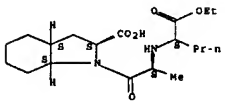
RN 690267-97-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

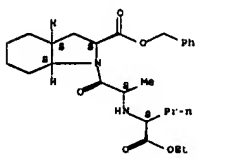
IT 122454-52-8P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and purification of η crystal form of perindopril erbumine of high purity and good solubility)

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester,

(2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

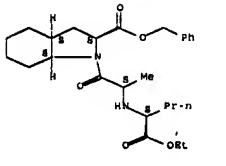


IT 924637-23-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and purification of η crystal form of perindopril erbumine of high purity and good solubility)

RN 924637-23-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, hydrochloride (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L6 ANSWER 28 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:175533 CAPLUS Full-text

DN 146:236293

TI Preparation of novel crystalline form of perindopril erbumine monohydrate

IN Ujagare, Ashish; Kochrekar, D. A.; Sarjekar, Pushpalata

PA Arch Pharmalabs Limited, India

SO PCT Int. Appl., 21pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007017893	A2	20070215	WO 2006-IN155	20060504
	WO 2007017893	A3	20070510		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI IN 2005-MU562 A 20050505

AB The present invention relates to a novel crystalline form of perindopril erbumine monohydrate exhibiting characteristic 2θ values and having purity not less than 99.8%. More particularly, the present invention relates to a process for the preparation of the novel cryst . form of perindopril erbumine monohydrate comprising steps of (i) dissolving perindopril erbumine in water; (ii) extracting the solution with toluene or xylene; (iii) removing water from the aqueous layer obtained from step (i); adding a polar solvent to the mass obtained from step (ii) at 20 to 45°; and (iv) filtering off the solid obtained.

IT 690267-97-1P, Perindopril erbumine monohydrate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation and purification of crystalline form of perindopril erbumine monohydrate of high purity)

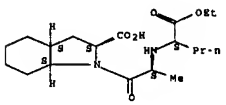
RN 690267-97-1 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

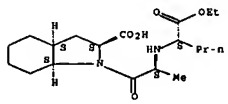
CRN 75-64-9
CMF C4 H11 N

IT 107133-36-8P, Perindopril erbumine
RL: PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation and purification of crystalline form of perindopril erbumine monohydrate of high purity)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



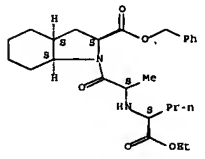
CM 2

CRN 75-64-9
CMF C4 H11 N

IT 122454-52-8P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic

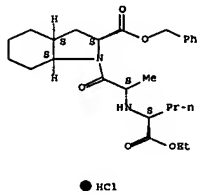
preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and purification of crystalline form of perindopril erbumine monohydrate of high purity)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



IT 924637-23-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and purification of crystalline form of perindopril erbumine monohydrate of high purity)
RN 924637-23-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, hydrochloride (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 29 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:174003 CAPLUS Full-text
DN 146:236108
TI Process for the preparation of crystalline perindopril

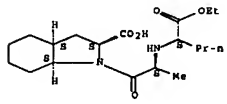
IN Jenko, Branko; Kopar, Anton
PA Lek Pharmaceuticals D.D., Slovenia
SO PCT Int. Appl., 28pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007017087	A1	20070215	WO 2006-EP7258	20060724
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI SI 2005-214	A	20050725		

AB The present invention relates to a new process for the preparation of crystalline perindopril. The present invention also relates to new alkyl ammonium salts of perindopril and the processes for the preparation thereof. A pharmaceutical composition comprising a therapeutically effective amount of high pure crystalline perindopril or perindopril alkyl ammonium salts or inclusion complexes of perindopril or perindopril alkyl ammonium salts with cyclodextrins or their alkylated and hydroxyalkylated derivs. are also claimed. Thus, (2S,3aS,7aS)-2-carboxyperhydroindole benzyl ester was treated with N-((S)-1-carbetoxybutyl)-(S)-alanine in acetonitrile in presence of O-(benzotriazol-1-yl)-N,N,N',N'- tetramethyluronium to afford perindopril benzyl ester in yield of 88%. Hydrogenolysis of the latter over 10% Pd/C yielded crude perindopril. Crude perindopril obtained was treated with tert-octylamine affording crystalline tert-octylammonium salt of perindopril in yield of 78%. Pure perindopril was precipitated from the crystalline tert-octylammonium salt of perindopril in presence of sulfuric acid and extracted with diisopropyl ether as solid glassy material.

IT 82834-16-0P, Perindopril 924264-24-4P
924264-25-5P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and compns. of crystalline perindopril and its alkyl ammonium salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

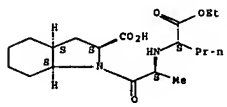


RN 924264-24-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2,2-dimethyl-1-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

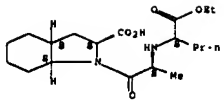
CRN 5813-64-9
CMF C5 H13 N

RN 924264-25-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2,4,4-trimethyl-2-pentanamine (1:1) (CA INDEX NAME)

CM 1

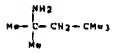
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 107-45-9
CMF C8 H19 N

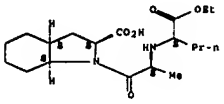


IT [illegible] PP, Perindopril erbumine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and compns. of crystalline perindopril and its alkyl ammonium salts)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

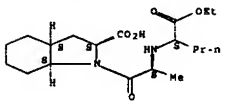
CRN 75-64-9
CMF C4 H11 N

IT 924264-23-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and compns. of crystalline perindopril and its alkyl ammonium salts)
RN 924264-23-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, benzoate (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



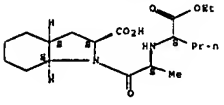
CM 2

CRN 65-85-0
CMF C7 H6 O2

IT 82834-16-0D, Perindopril, inclusion complexes with cyclodextrins
924264-24-4D, inclusion complexes with cyclodextrins
924264-25-5D, inclusion complexes with cyclodextrins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and compns. of crystalline perindopril and its alkyl ammonium salts)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

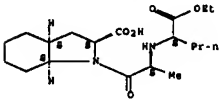


RN 924264-24-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2,2-dimethyl-1-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

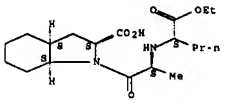
CRN 5813-64-9
CMF C5 H13 N

RN 924264-25-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2,4,4-trimethyl-2-pentanamine (1:1) (CA INDEX NAME)

CM 1

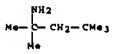
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 107-45-9
CMF C8 H19 N

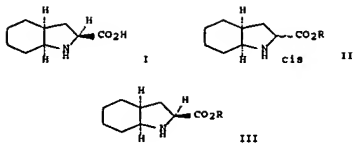


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 30 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:150959 CAPLUS Full-text
DN 146:206198
TI Process for the preparation of intermediates of perindopril
IN Joshi, Narendra Shriram; Ramam, Buddhavarapu Pattabhi; Bodkhe, Arjun Rajaram
PA Glenmark Pharmaceuticals Limited, India
SO U.S. Pat. Appl. Publ., 7pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2007032661	A1	20070208	US 2006-495102	20060728
	IN 2005MU00903	A	20070706	IN 2005-MU903	20050803
PRAI	IN 2005-MU903	A	20050803		
	US 2005-713000P	P	20050831		

OS CASREACT 146:206198; MARPAT 146:206198
GI



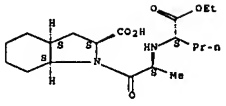
I cis II III

AB A process for the preparation of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid (I) is provided comprising (a) esterifying a cis-perhydroindole-2- carboxylic acid (II) with a first alc. of the formula ROH and a suitable free acid to provide the acid salt II.AS (Ad = acid), (b) reacting the acid salt with a first base to provide an ester (III), (c) treating the product of step (b) with an L-tartaric containing acid in a second alc. of the formula ROH to precipitate an ester salt III.L-tartarate, (d) reacting the ester salt with a second base to provide an ester III, and (e) hydrolyzing the ester to provide the desired compound I. Thus, cis-perhydroindole-2- carboxylic acid was esterified with benzyl alc. in the presence of p-toluenesulfonic acid under refluxing with azeotropic removal of water to give benzyl perhydroindole-2-carboxylate p-toluenesulfonate which was treated with triethylamine in CH2Cl2 to give benzyl cis-perhydroindole-2- carboxylate (IV). A solution of IV with methanol was treated with a solution of dibenzoyl-L-tartaric acid in methanol and the resulting mixture was stirred at 25° for .apprx.30 min, heated at .apprx.60° for .apprx.1 h, and cooled to 15°, followed by filtering the precipitated solid and drying at .apprx.60° to give benzyl (2S,3aS,7aS)-perhydroindole-2- carboxylate L-tartarate (V). V was added to CH2Cl2, treated with aqueous NaOH solution, stirred for 1 h to give, after workup, benzyl (2S,3aS,7aS)- perhydroindole-2-carboxylate which was refluxed in a NaOH/aqueous methanol solution for .apprx.2 h, adjusted to pH .apprx.6 to .apprx.7 with dilute aqueous HCl solution, concentrated, treated with ethanol, refluxed, filtered to remove inorgs., and concentrated to give I. I was converted into perindopril tert-butylamine salt which is a prodrug for perindoprilat (angiotensin converting enzyme inhibitor) and used to treat hypertension.

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril tert-butylamine salt
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid as intermediate for perindopril)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

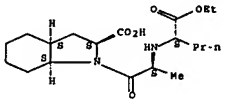


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L8 ANSWER 31 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:98910 CAPLUS Full-text
DN 146:434654
TI Reduction in Arterial Stiffness With Angiotensin II Antagonism and Converting Enzyme Inhibition
AU Rehman, Asia; Ismail, Shaiful Bahari; Naing, Lin; Roshan, Tariq Mahmood; Rahman, Abdul Rashid Abdul
CS School of Dental Sciences, University Sains Malaysia, Kelantan, Malay.
SO American Journal of Hypertension (2007), 20(2), 184-189

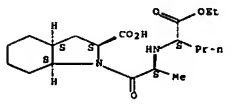
CODEN: AJHYE6; ISSN: 0895-7061
PB Elsevier Inc.
DT Journal
LA English

AB Background: Data comparing the effect of losartan and perindopril on aortic stiffness among hypertensive subjects without A1166C polymorphism was not available. Methods: The short-term and long-term effects of losartan (50 mg) and perindopril (4 mg) on aortic stiffness measured as carotid femoral pulse wave velocity (PWV) were compared in 39 middle-aged Malay subjects with mild-to-moderate hypertension in a 4-mo, double-blind, randomized, controlled, parallel-design study. Results: Four-month treatment with both drugs showed a significant reduction in blood pressure (BP) ($P < .005$) and PWV ($P < .05$) as compared to the baseline. On the other hand 1-mo treatment showed a significant reduction in BP only in perindopril group ($P < .05$) but not in the losartan group. There was no significant reduction in pulse pressure and PWV after 1 mo treatment by both drugs. No significant difference was seen in reduction in BP after 1 mo and 4 mo treatment between the two drugs. Similarly no significant difference was seen in reduction in PWV between the two drugs after 1 mo ($P = .613$) and 4 mo ($P = .521$) of treatment. Reduction in PWV by losartan ($r = 0.470$) and perindopril ($r = 0.457$) correlated significantly only with reduction in DBP ($P < .05$) and remained significant even after controlling for reduction in DBP ($P < .05$). Reduction in PWV by both losartan and perindopril was independent of reduction in BP by these drugs. Conclusions: These results showed that long-term treatment with losartan shows similar pressure independent reduction in PWV as perindopril among Malay hypertensive subjects with a homogenous "AA" genotype for angiotensin II type 1 receptor and may serve as a suitable alternative to perindopril.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiotensin converting enzyme inhibitor perindopril reduced arterial stiffness as was evident by reduction in carotid femoral pulse wave velocity in hypertensive Malay patient without ATIR A1166 polymorphism)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 32 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:91096 CAPLUS Full-text
DN 146:184735
TI Process for manufacture of (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (perindopril) and its tert-butyl amine salt
IN Gunjal, Sanjay Tukaram; Jadhav, Dilip Uttam; Kumar, Ashok; Arpana, Mathur; Panda, Nalinakshya Balaram; Soudagar, Satish Rajanikant
PA India
SO U.S. Pat. Appl. Publ., 10 pp., Cont.-in-part of U.S. Ser. No. 140,226.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2007021490	A1	20070125	US 2006-324349	20060103
IN 2005MU00017	A	20060811	IN 2005-MU17	20050106
US 2006178422	A1	20060810	US 2005-140226	20050527
PRAI IN 2005-MU17	A	20050106		
US 2005-140226	A2	20050527		
IN 2004-MU566	A	20040518		

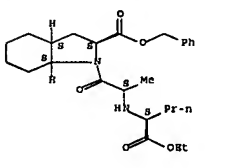
OS CASREACT 146:184735; MARPAT 146:184735

AB The invention relates to the preparation of perindopril [(2S,3aS,7aS)-1-[(2S)-2- [(S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid], its salts, and its novel intermediates, specifically aralkyl ester salts. Thus, (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid was treated with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine in CH2Cl2 in the presence of Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to afford 99% perindopril benzyl ester. Conversion of the latter into the oxalate salt, followed by hydrogenolysis over 5% Pd/C and reaction with tert-butylamine yielded perindopril erbumine.

IT 122454-52-8P 897922-11-1P 897922-12-2P 897922-13-3P 897922-14-4P 897922-15-5P 897922-16-6P 897922-18-8P 897922-19-9P 897922-20-2P 897922-21-3P 897922-22-4P 897922-23-5P 897922-24-6P 897922-25-7P 897922-26-8P 897922-27-9P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for synthesis of perindopril, its salts and its aralkyl ester salt intermediates)

RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

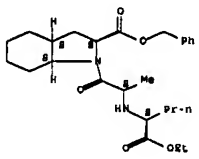


RN 897922-11-1 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

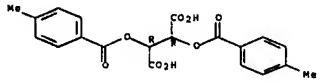
Absolute stereochemistry.



CM 2

CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).

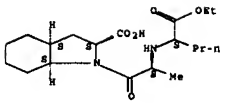


RN 897922-12-2 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

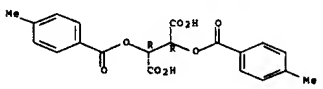
Absolute stereochemistry. Rotation (-).



CM 2

CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).

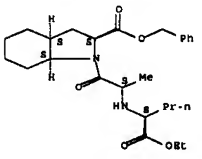


RN 897922-13-3 CAPLUS
CN Butanedioic acid, 2,3-dihydroxy- (2R,3R)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

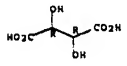
Absolute stereochemistry.



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

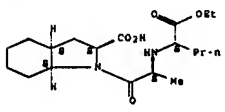


RN 897922-14-4 CAPLUS
CN Butanedioic acid, 2,3-dihydroxy- (2R,3R)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

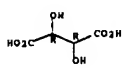
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

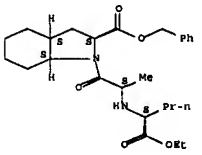


RN 897922-15-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, phosphate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

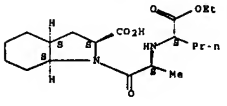
CRN 7664-38-2
CMF H3 O4 P

RN 897922-16-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, phosphate (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

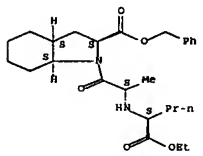
CRN 7664-38-2
CMF H3 O4 P

RN 897922-18-8 CAPLUS
CN 1,2-Benzenedicarboxylic acid, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

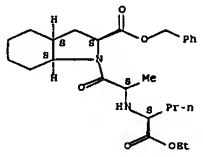
CRN 88-99-3
CMF C8 H6 O4

RN 897922-19-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, (1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

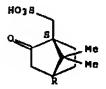
Absolute stereochemistry.



CM 2

CRN 3144-16-9
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).

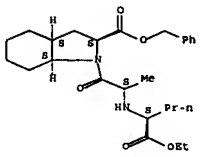


RN 897922-20-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:?) (CA INDEX NAME)

CM 1

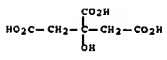
CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

CRN 77-92-9
CMF C6 H8 O7

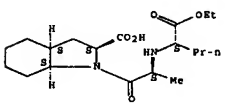


RN 897922-21-3 CAPLUS
CN 1,2-Benzenedicarboxylic acid, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

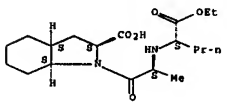
CRN 88-99-3
CMF C8 H6 O4

RN 897922-22-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, (1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonate (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

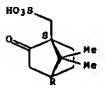
Absolute stereochemistry. Rotation (-).



CM 2

CRN 3144-16-9
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).

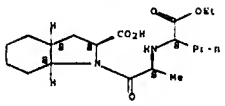


RN 897922-23-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:?) (CA INDEX NAME)

CM 1

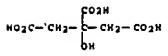
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 77-92-9
CMF C6 H8 O7

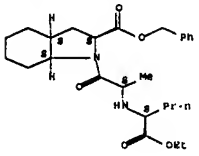


RN 897922-24-6 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

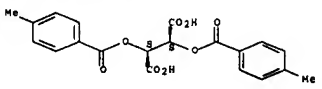
Absolute stereochemistry.



CM 2

CRN 32634-68-7
CMF C20 H18 O8

Absolute stereochemistry. Rotation (+).

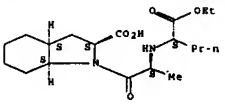


RN 897922-25-7 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

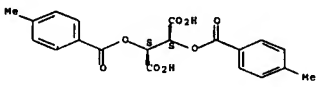
Absolute stereochemistry. Rotation (-).



CM 2

CRN 32634-68-7
CMF C20 H18 O8

Absolute stereochemistry. Rotation (+).



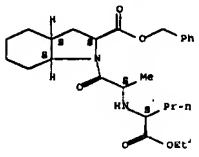
RN 897922-26-8 CAPLUS
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-rel-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-

1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

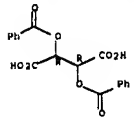
Absolute stereochemistry.



CM 2

CRN 22333-70-6
CMF C18 H14 O8

Relative stereochemistry.

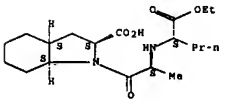


RN 897922-27-9 CAPLUS
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-rel-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

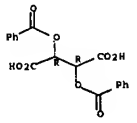
Absolute stereochemistry. Rotation (-).



CM 2

CRN 22333-70-6
CMF C18 H14 O8

Relative stereochemistry.

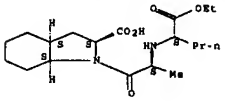


IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for synthesis of perindopril, its salts and its aralkyl ester salt intermediates)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

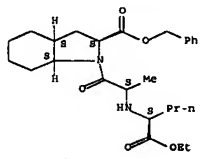
CRN 75-64-9
CMF C4 H11 N

IT 897922-09-7 897922-10-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for synthesis of perindopril, its salts and its aralkyl ester salt intermediates)
RN 897922-09-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, ethanedioate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

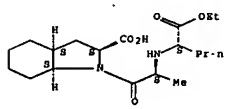
CRN 144-62-7
CMF C2 H2 O4

RN 897922-10-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, ethanedioate (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 144-62-7
CMF C2 H2 O4

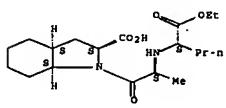
AN 2007:33054 CAPLUS Full-text
DN 146:122305
TI Process for the preparation of perindopril
IN Nath, Asok; Prasad, Mohan
PA Ranbaxy Laboratories Limited, India
SO PCT Int. Appl., 17pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007004165	A2	20070111	WO 2006-IB52191	20060629
WO 2007004165	A3	20070322		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRAI IN 2005-DE1694 A 20050630
OS CASREACT 146:122305
AB An improved process for the preparation of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] comprises treating silylated (2S,3aS,7aS)-2-carboxyperhydroindole with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanyl chloride hydrochloride. In an example, silylation of (2S,3aS,7aS)-2-carboxyperhydroindole was carried using hexamethyldisilazane and imidazole in methylene chloride. Crude perindopril was converted to perindopril tert-butylamine salt.
IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril by acylation of silylated carboxyperhydroindole)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

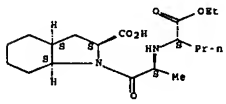


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



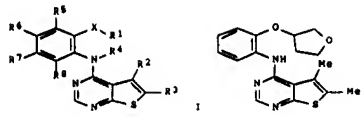
CM 2

CRN 75-64-9
CMF C4 H11 N

AN 2006:1354230 CAPLUS Full-text
DN 146:100711
TI Thienopyrimidines for pharmaceutical compositions and their preparation and use as kinase inhibitors
IN Jaekel, Stefan; Murfin, Stefen; Taylor, Steven; Aicher, Babette; Kelter, Arnd-Rene; Coulter, Thomasstefen
PA Developen Aktiengesellschaft, Germany
SO PCT Int. Appl., 180pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006136402	A1	20061228	WO 2006-EP5980	20060621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRAI EP 2005-13500 A 20050622
OS MARPAT 146:100711
GI



I II

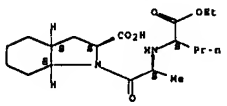
AB The invention relates to pharmaceutical compns. of formula I comprising thienopyrimidine compds. Compound of formula I wherein X is O, S, SO2, CH2, CO, NH and derivs., etc.; R1 - R3 are independently H, C1-6 alkyl, C1-6 alkyl-C3-10 (hetero)cycloalkyl, C3-10 cycloalkyl, C6-10 aryl, etc.; R4 is H, C1-4 alkyl, (thio)ureas, (un)substituted acetyl, 5- to 6-members heterocycle; R5- - R9 are independently H halo, CN, CO2H and derive., OH and derivs., CONH2 and derivs., SO2NH2 and derive.m etc.; and their metabolites, prodrugs and pharmaceutically acceptable salts thereof, are claimed. Moreover, the present invention relates to the use of the thienopyrimidine compds. of the invention for the production of pharmaceutical compns. for the prophylaxis and/or treatment of diseases which can be influenced by the inhibition of the kinase activity of Mnk1 and/or Mnk2 (Mnk2a or Mnk2b) and/or variants thereof. Example compound II was prepared by substitution of 2-fluoronitrobenzene with 3-hydroxytetrahydrofuran; the resulting 3-(2-nitrophenoxy)tetrahydrofuran underwent hydrogenation to give 3-(2-aminophenoxy)tetrahydrofuran, which underwent arylation with 4-chloro-5,6-dimethylthieno[2,3-d]pyrimidine. All the invention compds. were evaluated for their kinase inhibitory activity.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of thienopyrimidine compds. useful in prophylaxis and treatment of diseases)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 35 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1353979 CAPLUS Full-text

DN 146:101038
TI Process for industrially-viable preparation of perindopril erbumine
IN Potluri, Rameeh Babu; Venkata Subramanian, Hariharakrishnan; Mulakala, Acchuta Ramayya Chowdary; Kodali, Hari Prasad
PA India
SO PCT Int. Appl., 17pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006137082	A1	20061228	WO 2006-IN182	20060529
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2005CH00783	A	20070727	IN 2005-CH783	20050623
PRAI IN 2005-CH783	A	20050623		

OS CASREACT 146:101038; MARPAT 146:101038

AB A novel method for the preparation of perindopril erbumine [(2S,3aS,7aS)-1-[N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanyl]octahydro-1H-indole-2-carboxylic acid tert-butylamine salt] comprises treating (2S,3aS,7aS)-octahydro-1H- indole-2-carboxylic acid (I) esters with N-[(S)-1-(ethoxycarbonyl)butyl]-L- alanine, followed by deprotection and conversion to the erbumine salt. I benzyl ester hydrochloride was prepared from hexahydroindoline-2-carboxylic acid hydrochloride by catalytic hydrogenation, followed by esterification and resolution with dibenzoyl-L-tartaric acid or benzyloxycarbonyl-L-phenylalanine.

IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril erbumine)

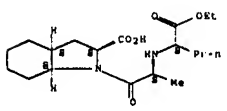
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

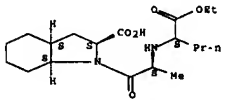
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 36 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1310975 CAPLUS Full-text
DN 146:45750
TI Process for the preparation of perindopril
IN Sinha, Brajesh Kumar; Vaddi, Pandu Ranga Rao; Budidet, Shankar Reddy; Dandala, Ramesh; Meenakshisunderam, Sivakumaran
PA Aurobindo Pharma Limited, India
SO PCT Int. Appl., 16pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006131828	A1	20061214	WO 2006-IB1583	20060601
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2005CH00703	A	20070727	IN 2005-CH703	20050608
IN 2005CH01355	A	20070928	IN 2005-CH1355	20050926
PRAI IN 2005-CH703	A	20050608		

IN 2005-CH1355 A 20050926
OS CASREACT 146:45750; MARPAT 146:45750
AB An improved process for the preparation of perindopril [(2S,3aS,7aS)-1-[(2S)-2- [(S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] comprises treating (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid benzyl ester p-toluenesulfonic acid salt with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine (e.g., in MeCN in the presence of 4-(dimethylamino)pyridine], followed by hydrogenolysis of perindopril benzyl ester over 5% Pd/C.
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

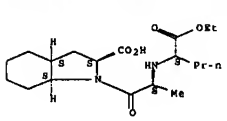


IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

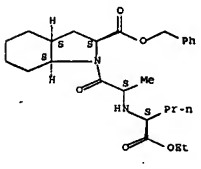


CM 2

CRN 75-64-9
CMF C4 H11 N

IT 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 37 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1252442 CAPLUS Full-text
DN 146:27826
TI Preparation of pyrazole compounds as hepatic glycogen phosphorylase inhibitors and therapeutic agents for diabetes
IN Takagi, Masaki; Nakamura, Takeshi; Matsuda, Isamu; Fukuda, Kenji; Ozawa, Koichi; Ueda, Nobuhisa; Sakata, Kaoru; Nomura, Yukihiro
PA Japan Tobacco Inc., Japan
SO PCT Int. Appl., 490pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

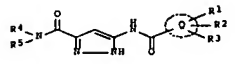
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006126695	A1	20061130	WO 2006-JP310603	20060522

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

JP 2007191461	A	20070802	JP 2006-141015	20060522
US 2007032529	A1	20070208	US 2006-438489	20060523
PRAI JP 2005-148847	A	20050523		
US 2005-685037P	P	20050526		
JP 2005-367286	A	20051220		
US 2006-755820P	P	20060103		

OS MARPAT 146:27826
GI

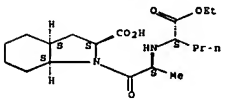


AB The title compds. (I) or pharmacol. acceptable salts thereof [ring Q = aryl or aromatic heterocyclic group; R1 = H, halo, C1-6 alkyl, C1-6 alkoxy; R2 = halo, C1-6 alkyl, C1-6 alkoxy, azido; R3 = halo, hydroxyl, C1-6 alkyl, halo-C1-6 alkyl, C1-6 alkoxy, azido, amino, acylamino, C1-6 alkylsulfonylamino; R4, R5 independently = H, C2-6 alkenyl, C2-6 alkynyl, (un)substituted C1-6 alkyl, C3-8 cycloalkyl, C3-8 cycloalkyl-C1-6 alkyl, 5- or 6-membered saturated monocyclic heterocyclic group, aryl, C7-14 C7-14 aralkyl, or 5- or 6-membered aromatic monocyclic heterocyclic group optionally fused to a benzene ring, etc.] are prepared These compds. have a hepatic glycogen phosphorylase inhibitory activity and therefore is useful as a therapeutic or prophylactic agent for diabetes. Thus, 6.00 g 5-(2-chloro-4,5-difluoro-benzoylamino)-1H-pyrazole-3-carboxylic acid imidazolide was suspended in 50 mL DMF, treated with 1.72 mL 3-picolylamine under ice-cooling, and stirred at room temperature overnight to give 4.49 g 5-(2-chloro-4,5-difluoro-benzoylamino)-1H-pyrazole-3-carboxylic acid N-(pyridin-3-ylmethyl)amide (II). II showed IC50 of <100 nm against human hepatic glycogen phosphorylase.
IT 107133-36-8, Perindopril Erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pyrazole compds. as hepatic glycogen phosphorylase inhibitors and therapeutic agents for diabetes)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 38 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1226928 CAPLUS Full-text
DN 145:505259
TI Preparation of 4-biarylyl-1-phenylazetidin-2-ones for the treatment of hypercholesterolemia
IN Antonelli, Stephen; Barden, Timothy C.; Cali, Brian; Currie, Mark G.; Lundrigan-Soucy, Regina; Yang, Jing-Jing; Yorgey, Peter S.; Zimmer, Daniel P.; Martinez, Eduardo; Schairer, Wayne C.; Talley, John J.
PA Microbia, Inc., USA
SO PCT Int. Appl., 449pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

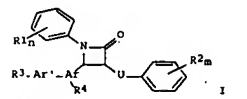
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006124713	A2	20061123	WO 2006-US18616	20060515
WO 2006124713	A3	20070118		

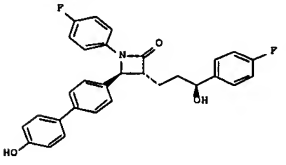
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-681232P	P	20050513		
US 2005-695988P	P	20050701		

OS MARPAT 145:505259
GI

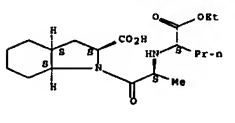




II

AB 4-Biaryl-1-phenylazetidin-2-ones of formula I [R1-R4 = H, halo OH, alkyl, alkoxy, CN, etc.; n, m = 1-5; U = alkylene, etc.; Ar = aryl, heteroaryl; Ar' = aryl] are prepared which are useful for the treatment of hypercholesterolemia. Thus, II was prepared, and had ED50 value of 0.002 mg/kg in rat cholesterol absorption model.
IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-drug; preparation of biarylphenylazetidinones for treatment of hypercholesterolemia)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

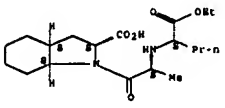


L6 ANSWER 39 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1177333 CAPLUS Full-text
DN 145:495604
TI Combination of a HMG-CoA reductase inhibitor and a drug intervening in the renin-angiotensin system for treating respiratory disorders
IN Lindmark, Bertil; Thoren, Anders; Higenbottam, Timothy William
PA Astrazeneca AB, Swed.; Astrazeneca UK Limited
SO PCT Int. Appl., 21pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006117534	A2	20061109	WO 2006-GB1582	20060428
WO 2006117534	A3	20070125		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
PRAI GB 2005-8924	A	20050430		

AB The invention provides medicaments comprising a combination of a HMG-CoA reductase inhibitor and a drug intervening in the renin-angiotensin system selected from angiotensin II antagonists and angiotensin converting enzyme (ACE) inhibitors optionally in combination with a bronchodilator and a glucocorticosteroid in the treatment of respiratory disorders such as chronic obstructive pulmonary disease (COPD).
IT [illegible], Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of a HMG-CoA reductase inhibitor and a drug intervening in the renin-angiotensin system for treating respiratory disorders)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

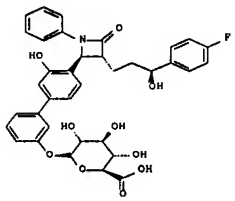
Absolute stereochemistry. Rotation (-).



L8 ANSWER 40 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1155934 CAPLUS Full-text
DN 145:465730
TI 4-Biarylyl-1-phenylazetidin-2-one glucuronide derivatives for hypercholesterolemia
IN Lundigran-Soucy, Regina
PA Microbia, Inc., USA; Martinez, Eduardo; Talley, John J.
SO PCT Int. Appl., 209pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006116499	A1	20061102	WO 2006-US15814	20060426
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
PRAI US 2005-674729P	P	20050426		

OS CASREACT 145:465730; MARPAT 145:465730
GI

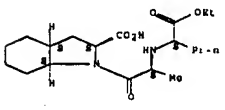


I

AB The invention relates to a chemical genus of 4-biarylyl-1-phenylazetidin-2-ones useful for the treatment of hypercholesterolemia and other disorders. E.g., I was prepared starting from 5-benzyl-1-(5-(4-fluorophenyl)-5-

hydroxypentanoyl]oxazolidinone. Examples demonstrating hypolipemic and anticholesteremic activity of I and similar compds. were given, e.g., using the rat cholesterol absorption model.
IT 82834-16-0, Perindopril
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biarylyl(phenyl)azetidinone glucuronide derivs. preparation for hypercholesterolemia)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 41 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1117967 CAPLUS Full-text
DN 145:418947
TI Preparation of α-form crystals of perindopril erbumine
IN Tanba, Hiroyuki; Imai, Eiji
PA Shiono Chemical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2006290825	A	20061026	JP 2005-115676	20050413
PRAI JP 2005-115676		20050413		

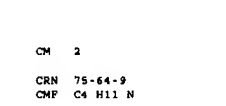
AB α-Form crystals of antihypertensive perindopril erbumine (α-I) is prepared by dissolving crude crystals of I in solvents and rapidly cooling the solution to a temperature lower than room temperature in the presence of seed crystals of α-I. Thus, crude crystals of 17.2 g I was dissolved in EtOAc upon heating to 78°, seed crystals were added, and the solution was cooled with an ice water to 4° over 10 min to give 13.0 g α-I.
IT 107133-36-8P, Perindopril erbumine
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); PREP (Preparation); PROC (Process)
(preparation of α-form crystals of perindopril erbumine by dissolving crude crystals in solvents and rapidly cooling the solution in the presence of seed crystals)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L8 ANSWER 42 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1097392 CAPLUS Full-text
DN 145:426033
TI Aerosol composition comprising non-ionic surfactant and phospholipid
IN Keller, Manfred; Friedrich, Ingo; Jauernig, Juergen; Lintz, Frank-Christophe
PA Pari G.m.b.H. Spezialisten fuer Effektive Inhalation, Germany
SO PCT Int. Appl., 72pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006108556	A2	20061019	WO 2006-EP3147	20060406
WO 2006108556	A3	20070503		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,			

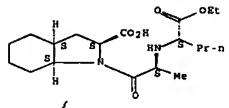
VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
EP 1712220 A1 20061018 EP 2005-8322 20050415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU
PRAI EP 2005-8322 A 20050415

AB Sterile compns. for administration as aerosols are described. They contain an active agent which is poorly water-soluble, a non-ionic surfactant component and a phospholipid component. The compns. are suitable for oral or nasal inhalation, but also for topical or mucosal administration. They are particularly useful for the efficient pulmonary administration of poorly soluble corticosteroids and can be aerosolized with common nebulizers. For example, tyloxapol 2 g, DMPC 2 g, and tocopherol acetate 20 mg were mixed with water 200 mL for injection and pre-homogenized with an Ultra Turrax. The dispersion was homogenized for about 15 min in a high-pressure homogenizer at 1500 bar. Reduced glutathione 2.5 g were rapidly dissolved in 50 mL of the resulting colloidal solution with stirring and the pH was adjusted to 6 by addition of lysine monohydrate. The resulting colloidal glutathione-vitamin E acetate solution was immediately sterile filtered into glass vials and subsequently freeze dried.

IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical aerosol composition comprising non-ionic surfactant and phospholipid)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

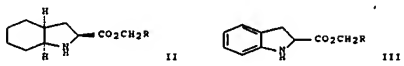


L8 ANSWER 43 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1038848 CAPLUS Full-text
DN 145:397363
TI Process for the synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its esters, useful intermediates in the manufacture of perindopril, via resolution of 2,3-dihydroindole-2-carboxylic acid alkyl esters and catalytic hydrogenation of (2S)-2,3-dihydroindole-2-carboxylic acid
IN Le, Goffic Francois
PA Laboratoire Substipharm, Fr.
SO Fr. Demande, 20pp.
CODEN: FRXXBL

DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 2883874	A1	20061006	FR 2005-3293	20050404
PRAI FR 2005-3293		20050404		

OS CASREACT 145:397363; MARPAT 145:397363
GI

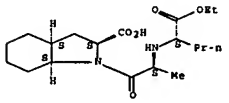


AB The invention is related to a process for preparation of (-)-(2S,3aS,7aS)-perhydroindole-2-carboxylic acid (I) and its esters II [R = H, alkyl], useful intermediates in the synthesis of perindopril, by (a) enzymic resolution of rac-III [R1 = (un)substituted H, alk(en)yl] by protease-catalyzed hydrolysis to isolate the ester (S)-III and (2R)-2,3-dihydroindole-2-carboxylic acid; (b) saponification or hydrolysis of the ester (S)-III to give (2S)-2,3-dihydroindole-2-carboxylic acid (IV); (c) catalytic hydrogenation of acid IV to give I; (d) isolation of acid I; (e) optionally, esterification of I to give esters of formula II; and (f) isolation of esters II. Advantages include selective preparation of diastereomer acid I in good yield and excellent purity, and simple purification Thus, acid I was prepared, in > 99% enantiomeric purity, via subtilisin-catalyzed resolution of a mixture of Me 2,3-dihydroindole-2- carboxylate and Et 2,3-dihydroindole-2-carboxylate and hydrogenation of acid IV over Rh/C.

IT 82834-16-0, Perindopril
RL: PNU (Preparation, unclassified)
(synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its esters as useful intermediates in the synthesis of perindopril)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

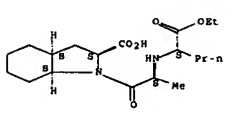
L8 ANSWER 44 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:983574 CAPLUS Full-text
DN 146:93014
TI Arterial hypertension: oxidative stress and endothelial disfunction
AU Vaskina, E.; Demin, A.; Tsyrendorjiev, D.; Pustovetova, M.
CS Novosibirsk State Medical Academy, Novosibirsk, 630091, Russia
SO Proceedings - KORUS 2004, Korea-Russia International Symposium on Science and Technology, 8th, Tomsk, Russian Federation, June 26-July 3, 2004 (2004), Volume 3, 361-363 Publisher: Institute of Electrical and Electronics Engineers, New York, N. Y.
CODEN: 69ILJH; ISBN: 0-7803-8383-4
DT Conference
LA English

AB The aim of the study was to investigate the pathogenetic significance of oxidative stress (OS) in the development of endothelial vascular dysfunction (ED) in essential arterial hypertension (AH) and to determine the possibilities of the markers usage for evaluation of antihypertensive drugs influence on leukocyte-endothelial interaction (LEI). Methods of research included evaluation of OS .apprx. oxidative metabolism of polymorphonuclear leukocytes (PML) by chemiluminescence (ChL), proinflammatory cytokines (interleukin-1β, TNF-α) by immunoenzyme methods, and ED, including evaluation of nitric oxide (NO) and hemostasis procoagulant factors. Results. It was revealed increased OS and ED in AH. In the frames of 4-wk randomized controlled clin. trial AT II receptors antagonist valsartan and ACE inhibitor perindopril, contrary to beta-adrenergic blocking agent atenolol, except achievement of target arterial pressure, normalize or considerably lower the raised oxidative stress and endothelial dysfunction, including proinflammatory cytokines and procoagulant factors activity, at arterial hypertension of 2-3 severity degrees with further delay of pathol. process progressing in patients. Conclusion. This investigation proves that the OS has important pathogenetic value for ED development at AH when arising damages of LEI conduct to proinflammation, vasoconstriction, prothrombosis, vascular remodeling and to defeat organs-targets.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(marker study show oxidative stress in endothelial vascular dysfunction in growth of arterial hypertension patient with LEI damage led to proinflammation, vasoconstriction, prothrombosis, vascular remodeling, organ-target defeat)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

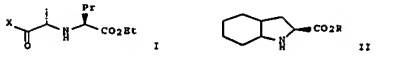
Absolute stereochemistry. Rotation (-).



L8 ANSWER 45 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:980040 CAPLUS Full-text
DN 145:357099
TI Process for the preparation of perindopril from ethoxycarbonylbutyl alanyl halide and carboxyperhydroindole
IN Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Rao, Kodali Eswara; Ramam, Buddhavarapu Pattabhi; Soni, Vijay
PA Glenmark Pharmaceuticals Limited, India
SO U.S. Pat. Appl. Publ., 6pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006211867	A1	20060921	US 2006-386011	20060321
US 7291745	B2	20071106		
IN 2005MU00306	A	20070608	IN 2005-MU306	20050321
PRAI IN 2005-MU306	A	20050321		
US 2005-666354P	P	20050330		

OS CASREACT 145:357099; MARPAT 145:357099
GI

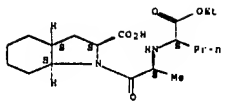


AB A process for preparing perindopril comprises condensing N-[(S)-1-ethoxycarbonylbutyl]-(S)-alanyl halides (I; X = halo) with (2S,3aS,7aS)-2-carboxyperhydroindoles (II; R = H, protecting group). Thus, N-[(S)-1-ethoxycarbonylbutyl]-(S)-alanyl chloride hydrochloride (preparation given) in CH2Cl2 at -5° was treated with imidazole and then with (2S,3aS,7aS)-2-carboxyperhydroindole followed by stirring at -5° to 0° for 2 h and at 20-25° for 2 h. Aqueous HOAc was added at <5° followed by stirring for 30 min. and separation and drying of the CH2Cl2 layer. This was treated with tert-butylamine at <10° followed by stirring at 35-40°, distillation of CH2Cl2, addition of Me2CHOH, acetone, and MeCN, heating to 65-70°, and slow cooling to 5-10° to give perindopril erbumine of >99.5% purity.

IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril from ethoxycarbonylbutyl alanyl halide and carboxyperhydroindole)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

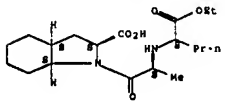


IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril from ethoxycarbonylbutyl alanyl halide and carboxyperhydroindole)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

IN Singh, Giri Pal; Godbole, Himanshu Madhav; Rananaware, Umesh Babanrao; Thube, Vilas Nathu; Tambe, Suhas Ganpat; Nehate, Sagar Purushottam
PA Lupin Limited, India
SO PCT Int. Appl., 23pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

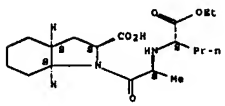
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006097941	A1	20060921	WO 2005-IN189	20050609
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
IN 2005MU00275	A	20070525	IN 2005-MU275	20050314
AU 2005329237	A1	20060921	AU 2005-329237	20050609
IN 2007MN01634	A	20071116	IN 2007-MN1634	20071008
PRAI IN 2005-MU275	A	20050314		
WO 2005-IN189	W	20050609		

AB The present invention relates to perindopril in the form of a salt with dicyclohexylamine, a process for its production and its use in the purification of a impure perindopril. The present invention also relates to preparation of perindopril tert-butylamine salt directly from perindopril dicyclohexylamine salt without isolating the free base. For example, perindopril 25 g was taken in acetonitrile 150 mL and stirred for about 10 min. The above solution was treated with dicyclohexylamine 5.2 g and stirred for about 8-10 h at room temperature The precipitated solid was filtered and washed with acetonitrile 20 mL. The dicyclohexylamine salt of perindopril 12 g was recrystd. in acetonitrile.
IT 909776-66-5P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(improved process for purification of perindopril)
RN 909776-66-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with N-cyclohexylcyclohexanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

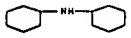
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 101-83-7
CMF C12 H23 N

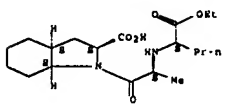


IT 107133-36-8P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(improved process for purification of perindopril)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

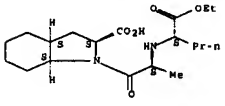


CM 2

CRN 75-64-9
CMF C4 H11 N

IT 82834-16-0, Perindopril
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(improved process for purification of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 47 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:821424 CAPLUS Full-text
DN 145:225771
TI Genetic markers in the HLA-C gene associated with an adverse hematological response to drugs
IN Aphanasiou, Maria; Gerson, Stanton
PA USA
SO U.S. Pat. Appl. Publ., 25pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006183146	A1	20060817	US 2006-351601	20060210
PRAI US 2005-652135P	P	20050211		

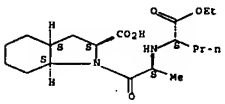
AB Genetic markers in the HLA-C gene associated with adverse hematol. response to drug therapy are disclosed. Compns. and methods for detecting and using these HLA-C markers in a variety of clin. applications are disclosed. Such applications include methods for testing an individual for susceptibility for an adverse hematol. response, methods of selecting the appropriate drug therapy for patients based on the presence or absence of a HLA-C marker, and products comprising a drug with hematol. toxicity that are approved for treating patients lacking a genetic marker.
IT 107133-36-8, Perindopril erbumine
RL: BSU (Biological study, unclassified); BUU (Biological use,

unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method and genstic markers based on HLA-C gene polymorphism
for predicting susceptibility to adverse hematol. response to drugs)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

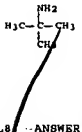
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



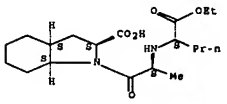
L8 ANSWER 48 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:796623 CAPLUS Full-text
DN 145:230528
TI Process for making highly pure perindopril erbumine
IN Kumar, Ashok; Soudagar, Satish Rajanikant; Mathur, Arpana; Shah, Chirag Hasmukh; Gunjal, Sanjay Tukaram; Metil, Dattatray Shamrao; Kelkar, Rahul Suresh; Thakare, Devendra Digambar; Kumar, Bindu Manoj; Nair, Raji
PA USA
SO U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006178422	A1	20060810	US 2005-140226	20050527
IN 2004MU00566	A	20060616	IN 2004-MU566	20040518

US 2007021490	A1	20070125	US 2006-324349	20060103
PRAI IN 2004-MU566	A	20040518		
IN 2005-MU17	A	20050106		
US 2005-140226	A2	20050527		

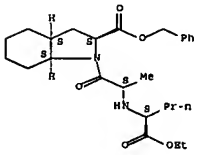
OS CASREACT 145:230528
AB A process for the synthesis and isolation of (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid and its tert-butylamine salt, comprises the amidation of (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester and N-[(S)1-carboxybutyl]-(S)-alanine Et ester in nonreactive solvents in turn avoiding the formation of the impurity N-acetyl (2S,3aS,7aS)- octahydroindole-2-carboxylic acid benzyl ester. The de-protection of benzyl ester group is optimized by catalytic hydrogenolysis and then isolation of the product from an aqueous layer by extraction using an organic solvent, which eliminates the need for lyophilization. This yields perindopril erbumins free of contaminants derivable from dicyclohexylcarbodiimide (e.g., dicyclohexylurea) and impurities originatsd by the use of Et acstate.
IT 82834-16-0P, Perindopril 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in a process for making highly pure perindopril erbumine)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

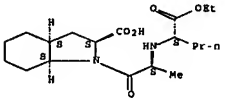


IT 107133-36-8P, Perindopril erbumine
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for making highly pure perindopril erbumine)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

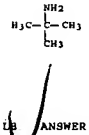
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L8 ANSWER 49 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:796580 CAPLUS Full-text
DN 145:224831
TI Genetic markers in the HLA-DQB1 gene associated with an adverse hematological response to drugs, and genotyping for drug risk assessment
IN Athanasiou, Maria; Gerson, Stanton
PA USA
SO U.S. Pat. Appl. Publ., 30pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

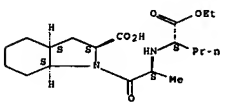
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006177860	A1	20060810	US 2006-351394	20060209
PRAI US 2005-651835P	P	20050209		

AB Genetic markers in the HLA-DQB1 gene associated with adverse hematol. response to drug therapy are disclosed. Compns. and methods for detecting and using these HLA-DQB1 markers in a variety of clin. applications are disclosed. Such applications include methods for testing an individual for susceptibility for an adverse hematol. response, methods of selecting the appropriate drug therapy for patients based on the presence or absence of a HLA-DQB1 marker, and products comprising a drug with hematol. toxicity that are approved for treating patients lacking a genetic marker.
IT 107133-36-8, Perindopril erbumine
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genetic markers in HLA-DQB1 gene associated with adverse hematol. response to drugs, and genotyping for drug risk assessment)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

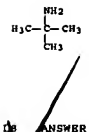
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L8 ANSWER 50 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:796329 CAPLUS Full-text
DN 145:224864
TI Hydroxylated nebivolol metabolites for treating and/or preventing vascular diseases
IN O'Donnell, John P.; Owens, Walter; Duncan, Joseph; Shaw, Andrew; Wu, Jinn
PA Mylan Laboratories, Inc., USA

SO PCT Int. Appl., 120pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006083779	A2	20060810	WO 2006-US3252	20060130
WO 2006083779	A3	20061123		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006210952	A1	20060810	AU 2006-210952	20060130
CA 2596426	A1	20060810	CA 2006-2596426	20060130
US 20070147313	A1	20070118	US 2006-342497	20060130
EP 1844024	A2	20071017	EP 2006-719896	20060130
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI US 2005-648551P	P	20050131		
US 2006-755056P	P	20060103		
WO 2006-US3252	W	20060130		

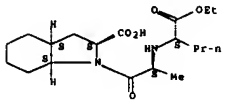
AB Hydroxylated nebivolol metabolites increase NO release from human endothelial cell preps. in a concentration dependent fashion following acute administration. In addition, hydroxylated nebivolol metabolites, including but not limited to 4-hydroxy-6,6'-difluoro-, 4-hydroxy-5-phenol-6,6'-difluoro-, and 4-hydroxy-5-phenol-6,6'-difluoro-, have the ability to increase the capacity for NO release in human endothelial cells following chronic administration. This invention provides hydroxylated nebivolol metabolites and compns. comprising nebivolol and/or at least one hydroxylated metabolite of nebivolol and/or at least one addnl. compound used to treat cardiovascular diseases or a pharmaceutically acceptable salt thereof. In addition, this invention provides methods of treating and/or preventing vascular diseases by administering at least one hydroxylated metabolite of nebivolol that is capable of releasing a therapeutically effective amount of nitric oxide to a targeted site affected by the vascular disease. Also, this invention is directed to the treatment and/or prevention of migraine headaches administering at least one hydroxylated metabolite of nebivolol. This invention may also be used in conjunction with or as a single treatment of metabolic syndrome disorders. Thus, acute treatment with six stereoselective hydroxy metabolites in endothelial cells from both white and black American donors showed that all six hydroxy metabolites have activity that was much superior to d-nebivolol, and most are superior to nebivolol racemats. As compared to nebivolol, the 4'-(R)-hydroxy-7-fluoro-6-hydroxy-1-nebivolol metabolite caused a nearly two-fold increase in NO release to 476 ± 20 and 383 ± 18 nmol/L, resp., from white and black donors. The 4'-(R)-hydroxy-5-fluoro-1-nebivolol metabolite also exceeded the activity of nebivolol and even 1-nebivolol by >80%. These findings indicate that hydroxy metabolites of nebivolol have distinct and highly reproducible effects on acute NO release in human endothelial cells.

IT [illegible], Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hydroxylated nebivolol metabolites for increase of NO release from endothelium in combination with other agent(s) for treating and/or preventing vascular diseases)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 51 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:796152 CAPLUS Full-text
DN 145:224029
TI Genetic markers in the CSF2RB gene associated with an adverse hematological response to drugs
IN Athanasiou, Maria; Gerson, Stanton
PA USA
SO U.S. Pat. Appl. Publ., 38pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006178843	A1	20060810	US 2006-351371	20060209
AU 2006213677	A1	20060817	AU 2006-213677	20060209
CA 2597259	A1	20060817	CA 2006-2597259	20060209
WO 2006086748	A2	20060817	WO 2006-US4960	20060209
WO 2006086748	A3	20061221		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1853909	A2	20071114	EP 2006-734885	20060209
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI US 2005-651834P	P	20050209		
WO 2006-US4960	W	20060209		

AB Genetic markers associated with adverse hematol. response to drug therapy are disclosed in the CSF2RB gene encoding β-chain of colony-stimulating factor 2 receptor. Compns. and methods for detecting and using these CSF2RB markers in a variety of clin. applications are disclosed. Such applications include methods for testing an individual for susceptibility for an adverse hematol. response, methods of selecting the appropriate drug therapy for patients based on the presence or absence of a CSF2RB marker, and products comprising a drug with hematol. toxicity that are approved for treating patients lacking a genetic marker.

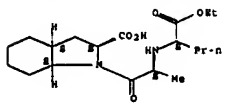
IT 107133-36-8, Perindopril erbumine
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(genetic markers in CSF2RB gene associated with adverse hematol. response to drugs, and genotyping for drug risk assessment)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

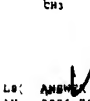
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



L8 ANSWER 52 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:796048 CAPLUS Full-text
DN 145:230398
TI 1-Acylamino-2-hydroxy-3-amino-w-arylalkanes as renin inhibitors and their preparation, pharmaceutical compositions and their use for treatment of hypertension

IN Mcgeehan, Gerard; Simpson, Robert D.; Zeng, Wenguang; Baldwin, John J.; Claremon, David A.; Dillard, Lawrence W.; Ishchenko, Alexey V.; Yuan, Jing; Xu, Zhenrong; Cagatian, Slavation; Tice, Colin; Zhao, Wei
PA Vitae Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 149pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006083924	A1	20060810	WO 2006-US3489	20060201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2596444	A1	20060810	CA 2006-2596444	20060201
EP 1844002	A1	20071017	EP 2006-720036	20060201
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI US 2005-649361P	P	20050202		
WO 2006-US3489	W	20060201		

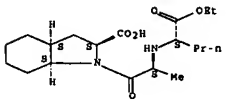
OS MARPAT 145:230398
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 1-Acylamino-2-hydroxy-3-amino-ω-arylalkanes of formula I and the salts thereof, have renin-inhibiting properties and can be used as antihypertensive, medicinally active ingredients. Compds. of formula I wherein R1 is H, Oh, halo, lower alkoxy, cycloalkoxy, etc.; R2 and R2 are independently H, halo, CN, carbamoyl, lower (halo)alkyl, etc.; R4 is H, lower alkyl, OH, lower alkoxy, cycloalkoxy, etc.; R2 and R3 or R3 and R4 taken together with the atoms they are attached form a fused (un)substituted dioxolane, (un)substituted dioxane, (un)substituted benzene or (un)substituted cyclohexene; R5 is lower (halo)alkyl, (halo)cycloalkyl, lower (halo)alkyl-cycloalkyl, aryl, heterocyclyl, etc.; R6 is amino, lower (di)alkylamino, or lower alkanoylamino; R7 is H, lower (halo)alkylcycloalkyl, or lower (halo)alkoxy-lower alkyl; X is methylene or hydroxymethylene; Q is CO, CS, or SO2; R8 is lower (halo)alkyl, C8-15 (halo)alkyl, (halo)cycloalkyl, lower alkyl-cycloalkyl, etc.; and the enantiomers, diastereoisomers and pharmaceutically acceptable salts thereof are claimed. Example compound II•HCl was prepared by aminolysis of compound III to give the corresponding diamino alc., which underwent amidation with cyclohexanecarboxylic acid to give tert-Bu (2S,3S,5S)-5-(3-(3-methoxypropoxy)-4-methoxybenzyl)-1-(cyclohexanecarbonyl)amino-2-hydroxy-6-methylheptan-3-ylcarbamate, which underwent acid hydrolysis to give compound II•HCl. All the invention compds. were evaluated for their renin inhibitory activity (no data).

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of acylamino(hydroxy)amino-ω-arylalkanes as renin-inhibitors useful as antihypertensive)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

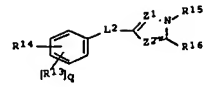


RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

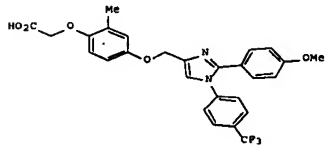
L8 ANSWER 53 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:795736 CAPLUS Full-text
DN 145:230633
TI Preparation of 4-[(benzimidazolyl/pyrazolyl/triazolyl)methoxy]phenoxyaceti c acids as PPAR modulators
IN Cow, Christopher; Epple, Robert; Wang, Xing; Xie, Yongping
PA Irm LLC, Bermuda
SO PCT Int. Appl., 62pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006084176	A2	20060810	WO 2006-US3924	20060203
	WO 2006084176	A3	20060914		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	AU 2006210503	A1	20060810	AU 2006-210503	20060203
	CA 2595789	A1	20060810	CA 2006-2595789	20060203
	EP 1843763	A2	20071017	EP 2006-734339	20060203
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

	IN 2007DN05903	A	20070817	IN 2007-DN5903	20070727
PRAI	US 2005-649962P	P	20050203		
	WO 2006-US3924	W	20060203		
OS	MARPAT 145:230633				
GI					



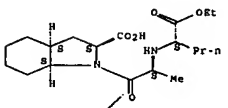
I



II

AB The title compds. I [q = 0-3; Z1, Z2 = CH, N; L2 = XOX, XSOO-2X, XSOO-2XO (wherein X = a bond, (un)substituted alkylene); R13 = halo, alkyl, alkoxy, etc.; R14 = XOXC(O)OR17, XC(O)OR17 (X = a bond, alkylene; R17 = H, alkyl); R15, R16 = R18 or YR18 (Y = alkylene, alkenylene, alkynylene, CONR17, OX; X = a bond, alkylene; R17 = H, alkyl; R18 = cycloalkyl, heterocycloalkyl, aryl, heteroaryl); or R15 and R16 together with the atoms to which R15 and R16 are attached form fused bicyclic or tricyclic heteroaryl], useful in treating or preventing diseases or disorders associated with the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPARδ (no specific data given), were prepared Thus, reacting Me (4-hydroxy-2-methylphenoxy)acetate with 4-(chloromethyl)-2-(4-methoxyphenyl)-1-(4-trifluoromethylphenyl)-1H- imidazole (prepns. given) followed by hydrolysis afforded 28% II. Also disclosed are pharmaceutical compns. comprising compds. I alone or in combination with other therapeutic agents.
IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 4-{(benzimidazolyl/pyrazolyl/triazolyl)methoxy]phenoxyacetic acids as PPAR modulators for treating and preventing diseases-associated with PPAR activity, particularly activity of PPARδ)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 54 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:680403 CAPLUS Full-text
DN 145:124844
TI Process for the synthesis of (2S,3aS,7aS)-1-(S)-alanyloctahydro-1H-indole-2-carboxylic acid derivatives and use in the synthesis of perindopril
IN Kumar, Ashok; Soudagar, Satish Rajanikant; Mathur, Arpana; Gunjal, Sanjay Tukaram; Panda, Nalinakanya Balaram; Jadhav, Dilip Uttam
PA IPCA Laboratories Limited, India
SO Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

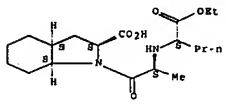
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1679072	A1	20060712	EP 2005-113099	20051230
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
	IN 2005MU00017	A	20060811	IN 2005-MU17	20050106
PRAI	IN 2005-MU17	A	20050106		
OS	CASREACT 145:124844				

AB The invention relates perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] aralkyl ester salts used in the synthesis of perindopril. Thus, (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid was treated with N-[(S)-1-(ethoxycarbonyl)butyl]-L-alanine in CH2Cl2 in the presence of Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to afford 99% perindopril benzyl ester. Conversion of the latter into the oxalate salt, followed by hydrogenolysis over 5% Pd/C and reaction with tert-butylamine yielded perindopril erbumine.
IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for synthesis of alanyloctahydroindolecarboxylic acid derivs. in synthesis of perindopril)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

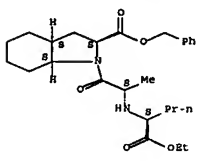


CM 2

CRN 75-64-9
CMF C4 H11 N

IT 122454-52-8P 897922-09-7P 897922-10-0P 897922-11-1P 897922-12-2P 897922-13-3P 897922-14-4P 897922-15-5P 897922-16-6P 897922-18-8P 897922-19-9P 897922-20-2P 897922-21-3P 897922-22-4P 897922-23-5P 897922-24-6P 897922-25-7P 897922-26-8P 897922-27-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for synthesis of alanyloctahydroindolecarboxylic acid derivs. in synthesis of perindopril)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

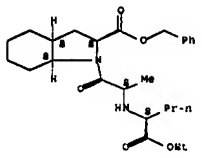


RN 897922-09-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, ethanedioate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

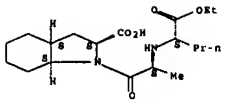
CRN 144-62-7
CMF C2 H2 O4

RN 897922-10-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, ethanedioate (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

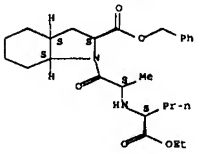
CRN 144-62-7
CMF C2 H2 O4

RN 897922-11-1 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

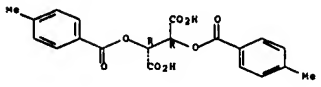
Absolute stereochemistry.



CM 2

CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).

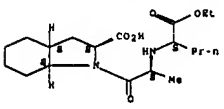


RN 897922-12-2 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

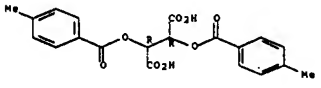
Absolute stereochemistry. Rotation (-).



CM 2

CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).



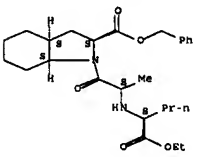
RN 897922-13-3 CAPLUS
CN Butanedioic acid, 2,3-dihydroxy- (2R,3R)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8

CMF C26 H38 N2 O5

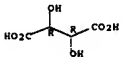
Absolute stereochemistry.



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

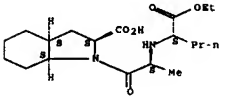


RN 897922-14-4 CAPLUS
CN Butanedioic acid, 2,3-dihydroxy- (2R,3R)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

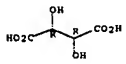
Absolute stereochemistry. Rotation (-).



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

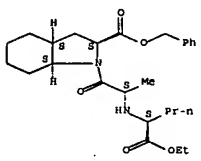


RN 897922-15-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, phosphate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

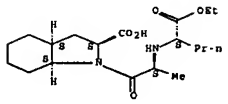
RN 897922-16-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-,

phosphate (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

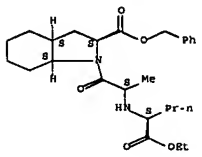
CRN 7664-38-2
CMF H3 O4 P

RN 897922-18-8 CAPLUS
CN 1,2-Benzenedicarboxylic acid, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

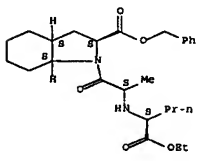
CRN 88-99-3
CMF C8 H6 O4

RN 897922-19-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, (1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

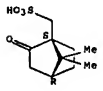
Absolute stereochemistry.



CM 2

CRN 3144-16-9
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).

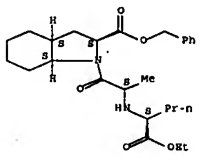


RN 897922-20-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:?) (CA INDEX NAME)

CM 1

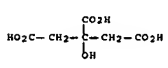
CRN 122454-52-8
CMF C26 H38 N2 O5

Absolute stereochemistry.



CM 2

CRN 77-92-9
CMF C6 H8 O7

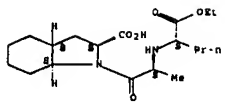


RN 897922-21-3 CAPLUS
CN 1,2-Benzenedicarboxylic acid, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

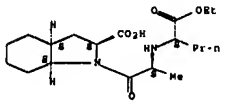
CRN 88-99-3
CMF C8 H6 O4

RN 897922-22-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, (1S,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-methanesulfonate (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

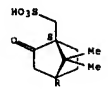
Absolute stereochemistry. Rotation (-).



CM 2

CRN 3144-16-9
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).

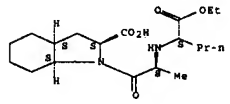


RN 897922-23-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, 2-hydroxy-1,2,3-propanetricarboxylate (1:?) (CA INDEX NAME)

CM 1

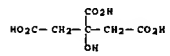
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 77-92-9
CMF C6 H8 O7

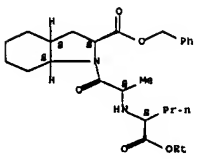


RN 897922-24-6 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

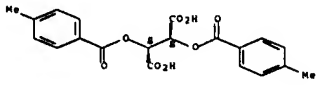
Absolute stereochemistry.



CM 2

CRN 32634-68-7
CMF C20 H18 O8

Absolute stereochemistry. Rotation (+).

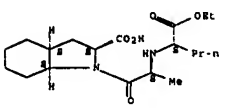


RN 897922-25-7 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2S,3S)-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:?) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

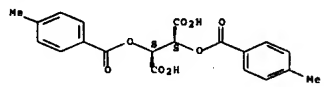
Absolute stereochemistry. Rotation (-).



CM 2

CRN 32634-68-7
CMF C20 H18 O8

Absolute stereochemistry. Rotation (+).

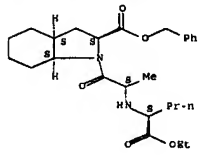


RN 897922-26-8 CAPLUS
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-rel-, compd. with phenylmethyl (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:?) (CA INDEX NAME)

CM 1

CRN 122454-52-8
CMF C26 H38 N2 O5

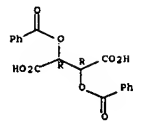
Absolute stereochemistry.



CM 2

CRN 22333-70-6
CMF C18 H14 O8

Relative stereochemistry.

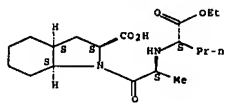


RN 897922-27-9 CAPLUS
CN Butanedioic acid, 2,3-bis(benzoyloxy)-, (2R,3R)-rel-, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid (1:7) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

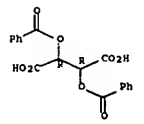
Absolute stereochemistry. Rotation (-).



CM 2

CRN 22333-70-6
CMF C18 H14 O8

Relative stereochemistry.



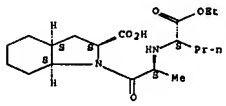
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 55 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:677768 CAPLUS Full-text
DN 145:122111
TI Genotyping of PECAM-1 polymorphisms associated with risk of atherosclerosis and coronary heart disease
IN Chatterjee, Subroto; Heming, Wei
PA The Johns Hopkins University, USA
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006074405	A2	20060713	WO 2006-US525	20060105
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2005-641595P	P	20050105		

AB The invention relates to methods of identifying inter-patient differences in genotype of PECAM-I to diagnose and assess risk of arterial disease. Two single nucleotide polymorphisms in the PECAM-1 gene, Leu125Val (c373g) and Ser563Asn (g1688a), are associated with coronary heart disease in an Asian Indian population. Ren cells transfected with wild-type and or 125-Val and 563-Asn gene polymorphism exhibit increased PECAM-1 protein levels associated with variant haplotype. The invention further relates to methods of identifying therapeutics agents for to treat coronary arterial disease, and to methods for determining and exploiting such differences to improve medical outcomes.
IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selection of and responsiveness to; genotyping of PECAM-1 polymorphisms associated with risk of atherosclerosis and coronary heart disease)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 56 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:655550 CAPLUS Full-text
DN 145:83667
TI Process for preparing perindopril erbumine
IN Palomo Nicolau, Francisco; De Leon, Dorcas
PA Quimica Sintetica, S.A., Spain
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

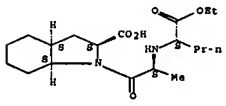
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006070276	A1	20060706	WO 2005-IB3928	20051216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
ES 2255872	A1	20060701	ES 2004-3168	20041231
ES 2255872	B1	20070816		
EP 1833788	A1	20070919	EP 2005-818419	20051215
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI ES 2004-3168	A	20041231		
WO 2005-IB3928	W	20051215		

OS CASREACT 145:83667
AB A process for preparing perindopril erbumine, useful in the treatment of hypertension, comprises reacting an active ester of N-[1(S)-(ethoxycarbonyl)butyl]-L-alanine with an organic salt of perhydroindole-2-carboxylic acid, followed by the addition of tert-butylamine. An example using the acetonoxime as active ester in acetonitrile in the presence of phosphacene afforded 90% perindopril erbumine (99.5% purity).
IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril erbumine)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

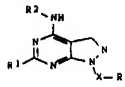
CRN 75-64-9
CMF C4 H11 N

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 57 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:634691 CAPLUS Full-text
DN 145:124588
TI Preparation of pyrazolopyrimidines as inhibitors of kinase activity
IN Coulter, Thomas Stephen; Taylor, Steven; Murfin, Stephen; Thammalaksa, Valery; Aicher, Babette; Haekel, Stefan; Reuter, Tanja
PA Developen Aktiengesellschaft, Germany; Evotec A.-G.
SO PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006066937	A2	20060629	WO 2005-EP13907	20051222
WO 2006066937	A3	20061019		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1746099	A1	20070124	EP 2004-30674	20041223
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU
EP 1827444 A2 20070905 EP 2005-822979 20051222
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
PRAI EP 2004-30674 A 20041223
WO 2005-EP13907 W 20051222
OS MARPAT 145:124588
GI



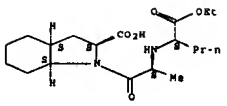
AB The present invention relates to the use of pyrazolopyrimidine compds. [I; R1 = substituted C6-10 aryl or optionally substituted C5-10 heteroaryl, wherein the substituents are one or more of R4; R4 = halogen, cyano, CO2R5, OR5, C(O)N(R5R5a), S(O)2N(R5R5a), S(O)N(R5R5a), S(O)2R5, N(R5)S(O)2N(R5R5a), SR5, N(R5R5a), OC(O)R5, N(R5)C(O)R5a, N(R5)S(O)2R5a, etc.; R5, R5a = H, C3-10 cycloalkyl, C4-10 bicycloalkyl, C4-10 heterocyclyl, (un)substituted C1-6 alkyl, etc.; R2 = H, C1-4 alkyl, acetyl, urea; R3 = H, hydroxy, C1-4 alkyl, amino; X = a bond] or metabolites, prodrugs or pharmaceutically acceptable salts thereof, and optionally a pharmaceutically acceptable carrier for the preparation of pharmaceutical compns. for inhibiting the activity of the kinase activity of Mnk1 or Mnk2 (Mnk2a, Mnk2b) or variants thereof or for the prophylaxis and/or treatment of diseases which can be influenced by the inhibition of the kinase activity of Mnk1 and/or Mnk2 (Mnk2a or Mnk2b) and/or variants thereof. The above diseases include diseases of the carbohydrate and/or lipid metabolism and their consecutive complications and diseases, e.g. impaired glucose tolerance, diabetes mellitus type II, latent autoimmune diabetes in adults (LADA), diabetes mellitus type I, obesity, metabolic syndrome, eating disorders, cachexia, osteoarthritis, biliary stones, and diabetic complications (carbohydrate metabolic diseases) and hypercholesterolemia, dislipidemia familial hypercholesterolemia, Fredrickson's hyperlipoproteinemia, and cardiovascular diseases (lipid metabolic diseases). Thus, [4-(pyrrol-1-yl)phenyl]hydrazine hydrochloride was treated with NaOEt in ethanol at room temperature and cyclocondensed with (ethoxymethylene)malononitrile under refluxing for 2 h to give 88% 5-amino-1-[4-(pyrrol-1-yl)phenyl]-1H-pyrazole-4-carbonitrile which was cyclocondensed with formamide at 180° for 3 h to give 11% [1-[4-(pyrrol-1-yl)phenyl]-1H-pyrazolo[3,4-d]pyrimidin-4-yl]amine (II).

IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of pyrazolopyrimidines as inhibitors of Mnk1 or Mnk2 (Mnk2a or Mnk2b) kinase activity)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 58 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:627685 CAPLUS Full-text
DN 145:89824
TI Preparation of perindopril erbumine crystal type I
IN Kiuchi, Yasuyuki; Yokogoshi, Kiyonori
PA Permachem Asia, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2006169169	A	20060629	JP 2004-364224	20041216
PRAI JP 2004-364224			20041216	

AB This invention relates to industrial manufacturing method for novel crystal type perindopril erbumine (I) with high purity and high yield. The I is treated with THF or perindopril is reacted with tert-butylamine in THF solvent to form crystalline I type I.

IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of perindopril erbumine crystal type I)

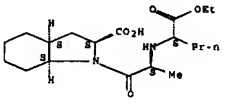
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

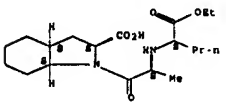
CRN 75-64-9
CMF C4 H11 N

IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of perindopril erbumine crystal type I)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 59 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:597465 CAPLUS Full-text
DN 146:100554
TI New procedure for preparation of perindopril in new crystal form
IN Rucman, Rudolf
PA Diagen D.O.O., Slovenia
SO Slov., 16pp.
CODEN: SIXXAW
DT Patent
LA Slovenian
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI SI 21801	A	20051231	SI 2004-181	20040621
PRAI SI 2004-181		20040621		

OS CASREACT 146:100554; MARPAT 146:100554

AB The submitted invention deals with a synthesis of the ACE inhibitor perindopril, starting from a stereospecific aminoacid N-((S)-carbethoxy-1-butyl)-(S)-alanine, which is protected with a trimethylsilyl group and then transformed into a reactive acidic bromide or fluoride which in the final

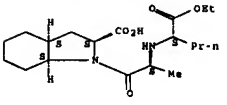
phase reacts with (2S,3aS,7aS)-octahydroindol-2-carboxylic acid with the trimethylsilyl protection on the carboxylic group to obtain perindopril after removal of protection groups.

IT 82834-16-0P, Perindopril
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of perindopril in new crystal form)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

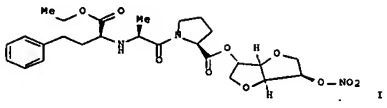
Absolute stereochemistry. Rotation (-).



L8 ANSWER 60 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:469692 CAPLUS Full-text
DN 144:460880
TI Nitrosated and nitrosylated compounds, compositions, and methods for the treatment of ophthalmic disorders
IN Letts, L. Gordon; Garvey, David S.
PA Nitromed, Inc., USA
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006052899	A2	20060518	WO 2005-US40314	20051108
WO 2006052899	A3	20061116		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2005304770	A1	20060518	AU 2005-304770	20051108
CA 2576279	A1	20060518	CA 2005-2576279	20051108
EP 1814535	A2	20070808	EP 2005-826100	20051108
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRAI US 2004-625578P P 20040108
WO 2005-US40314 W 20051108
OS MARPAT 144:460880
GI



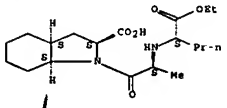
I

AB The invention describes nitrosated and/or nitrosylated compds. or pharmaceutically acceptable salts thereof, and compns. comprising at least one nitrosated and/or nitrosylated compound, and, optionally, at least one nitric oxide donor and/or at least one therapeutic agent. The invention also provides compns. and kits comprising at least one compound of the invention, that is optionally nitrosated and/or nitrosylated, and, optionally, at least one nitric oxide donor compound and/or at least one therapeutic agent. The invention also provides methods for treating ophthalmic disorders. The nitrosated and/or nitrosylated compds. are preferably nitrosated and/or nitrosylated adrenergic antagonists and nitrosated and/or nitrosylated angiotensin-converting enzyme (ACE) inhibitors. Preparation of I is described.

IT 82834-16-0P, Perindopril, nitrosated and nitrosylated derivs.
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitrosated and nitrosylated compds. for treatment of ophthalmic disorders)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L6 ANSWER 61 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:386591 CAPLUS Full-text
DN 144:412896

TI Preparation of perindopril precursor and perindopril erbumine
IN Kiuchi, Yasuyuki; Yokogoshi, Kiyonori
PA Permachem Asia, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2006111579	A	20060427	JP 2004-301012	20041015
PRAI JP 2004-301012		20041015		

OS MARPAT 144:412896
AB Perindopril p-methoxybenzyl ester (I) is prepared from (2S,3aS,7aS)-2-carboxyoctahydroindole (II) via BOC-II and its p-methoxybenzyl ester. Acid hydrolysis of I and treatment with Me3CNH2 give perindopril erbumine. Thus, protection of II with di-tert-Bu dicarbonate gave 91% BOC-II, which was esterified with p-ClCH2C6H4OMe to afford 92% p-methoxybenzyl ester. The ester was deprotected by methanesulfonic acid and amidated with (S)-EtO2CCHPr-L-Ala to give I.

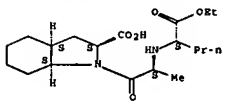
IT 107133-36-8P, Perindopril erbumine 793716-57-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril erbumine via p-methoxybenzyl ester)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

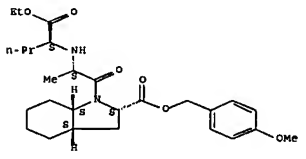


CM 2

CRN 75-64-9
CMF C4 H11 N

RN 793716-57-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (4-methoxyphenyl)methyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

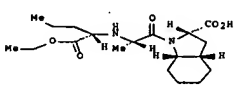
Absolute stereochemistry.



L8 ANSWER 62 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:356970 CAPLUS Full-text
DN 144:398255
TI Preparation of hydrated crystalline forms of perindopril erbumine and pharmaceutical formulations
IN Rucman, Rudolf; Zupet, Pavel
PA Diagen Smartno Pri Ljubljani, d.o.o., Slovenia
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1647547	A1	20060419	EP 2005-468015	20051013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
SI 21881	A	20060430	SI 2004-285	20041015
PRAI SI 2004-285	A	20041015		

GI



I

AB The object of the invention are new crystalline forms perindopril erbumine (I.Me3CNH2) monohydrate, I.Me3CNH2 sesquihydrate and I.Me3CNH2 dihydrate and a process for the preparation thereof by dissolving I.Me3CNH2 in water or in water with the addition of a volatile water-miscible polar organic solvent, freezing and lyophilizing. Another object of the invention is a new process for the preparation of perindopril erbumine monohydrate in pure crystalline form by freezing aqueous acetone solns. and lyophilizing. Another object of the invention are pharmaceutical formulations for the treatment of arterial hypertension and with vasodilatory activity, containing a therapeutically effective amount of these new crystalline forms.

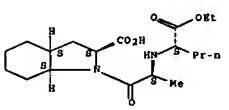
IT 107133-36-8, Perindopril erbumine 690267-97-1
982674-51-3 982674-53-5, Perindopril erbumine sesquihydrate
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of hydrated crystalline forms of perindopril erbumine and pharmaceutical formulations)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

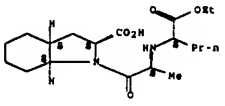
RN 690267-97-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd.

with 2-methyl-2-propanamine, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

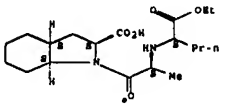
CRN 75-64-9
CMF C4 H11 N

RN 882674-51-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

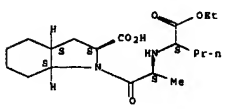
CRN 75-64-9
CMF C4 H11 N

RN 882674-53-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine, hydrate (2:2:3) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 63 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:342911 CAPLUS Full-text
DN 144:382027
TI Angiotensin receptor signal transduction inhibitors for treating

otosponglosis
IN Imauchi, Yutaka
PA Japan
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006038265	A1	20060413	WO 2004-JP14390	20040930

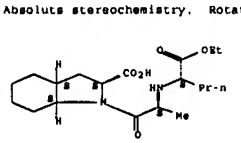
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI WO 2004-JP14390 20040930
AB It is intended to provide a medicinal composition for treating otospongiosis, a method of determining its dose, a method of administering the same and a diagnostic marker for otospongiosis. As a diagnostic marker for otospongiosis, DNA is isolated from a human subject and the genotype of the allele at the M235T polymorphism in angiotensinogen gene is examined by PCR. Based on the results thus obtained, the cause of otospongiosis is estimated In the case where otospongiosis is seemingly caused by the hyperactivity of an angiotensinogen receptor, a drug compound capable of lowering the activity is administered to the patient.
IT 107133-36-8, Perindopril erbumine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiotensin II receptor signal transduction inhibitors for treatment of otospongiosis)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 64 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:269508 CAPLUS Full-text
DN 144:331420
TI Preparation of bicyclic anilide spirolactam cgrp receptor antagonists
IN Bell, Ian M.; Theberge, Cory R.; Stump, Craig A.; Zhang, Xufang; Gallicchio, Steven N.; Zartman, C. Blair
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006031610	A2	20060323	WO 2005-US32041	20050909
WO 2006031610	A3	20060831		

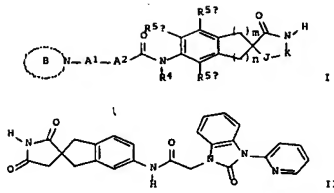
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2005285109	A1	20060323	AU 2005-285109	20050909
CA 2579847	A1	20060323	CA 2005-2579847	20050909
EP 1797073	A2	20070620	EP 2005-795448	20050909

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

CN 101018781	A	20070815	CN 2005-80030605	20050909
IN 2007DN01493	A	20070803	IN 2007-DN1493	20070223
PRAI US 2004-609292P	P	20040913		
WO 2005-US32041	W	20050909		

OS MARPAT 144:331420
GI



I

II

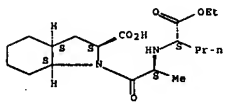
AB Title compds. I [A1 and A2 independently = bond or CR13R14, where one of A1 and A2 is optionally absent; B = (un)substituted bicycloheterocycle; J = =C(R6a)-; CR13R14, and CO; K = =C(R6b), CR13R14, CO, etc.; R4 = H, (un)substituted alkyl, benzyl, etc.; R5a, R5b, and R5c = H, alkyl, alkoxy, halo, etc.; R6a and R6b independently = H, OH, halo, (un)substituted alkyl, etc.; R13 and R14 = H or (un)substituted alkyl; m = 1 or 2; n = 1 or 2], and their pharmaceutically acceptable salts, useful as antagonists of calcitonin gene-related peptide (CGRP) receptors and useful in the treatment or prevention of diseases in which the CGRP is involved, such as headache, migraine and cluster headache. Thus, e.g., II was prepared by reaction of 5-amino-1,3-dihydro-2'H,5'H-spiro[indene-2,3'-pyrrolidine]- 2',5'-dione (preparation given) with 5-amino-1,3-dihydrospiro[indene-2,3'- pyrrolo[2,3-b]pyridin]-2'(1'H)-one (preparation given). I demonstrated activity as antagonists of the CGRP receptor with Ki or IC50 values generally less than about 50 μM. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which CGRP is involved.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substances for use in combination chemotherapy with bicyclic anilide spirolactam compds. in prevention and treatment of diseases associated with CGRP receptor)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

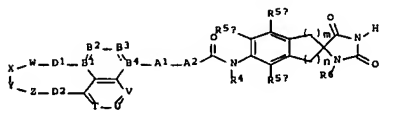
Absolute stereochemistry. Rotation (-).



L8 ANSWER 65 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:268948 CAPLUS Full-text
DN 144:331434
TI Preparation of tricyclic anilide spirohydantoin CGRP receptor antagonists
IN Bell, Ian M.; Gallicchio, Steven N.; Zartman, C. Blair; Theberge, Cory R.; Zhang, Xufang
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006031676	A2	20060323	WO 2005-US32288	20050909
WO 2006031676	A3	20070426		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
AU 2005285083	A1	20060323	AU 2005-285083	20050909
CA 2579850	A1	20060323	CA 2005-2579850	20050909
EP 1794146	A2	20070613	EP 2005-796599	20050909
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 101076527	A	20071121	CN 2005-80030477	20050909
IN 2007DN01494	A	20070803	IN 2007-DN1494	20070223
PRAI US 2004-609294P	P	20040913		
WO 2005-US32288	W	20050909		

OS MARPAT 144:331434
GI



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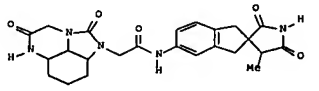


II

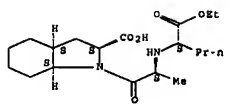
AB Title compds. I [A1 and A2 independently = bond or CR13R14, where one of A1 and A2 is optionally absent; B1 and B4 independently = C when double bond present, CR1 or N; B2 and B3 independently = bond, CR1R2, CO, CS, O, S, etc., where one of B2 and B3 is optionally absent; D1 and D2 independently = O, S, SO2, CR1R2, CO, etc.; T, U and V independently = =C(R1)- and =N-, wherein at least one of T, U, and V = =C(R1)-; W, X, Y, and Z = bond, CR1R2, CS, O, etc.; R1 and R2 = H, (un)substituted alkyl, cycloalkyl, alkynyl, etc.; R4 = H, (un)substituted alkyl, benzyl, etc.; R5a, R5b, and R5c = H, alkyl, alkoxy, halo, etc.; R6 = H, (un)substituted alkyl, cycloalkyl, etc.; R13 and R14 = H, OH, halo, and (un)substituted alkyl; m = 1 or 2; n = 1 or 2], and their pharmaceutically acceptable salts, useful as antagonists of calcitonin gene-related peptide (CGRP) receptors and useful in the treatment or prevention of diseases in which the CGRP is involved, such as headache, migraine and cluster headache. Thus, e.g., II was prepared by reaction of (-)-5'-amino-3-methylspiro[imidazolidine-4,2'-indane]-2,5-dione (preparation given) with sodium (2,5-dioxo-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin- 1(2H)yl)acetate (preparation given). I demonstrated activity as antagonists of the CGRP receptor with Ki or IC50 values generally less than about 50 μM. The invention is also directed to pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which CGRP is involved.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(substances for use in combination chemotherapy with tricyclic anilide spirolactam compds. in prevention and treatment of diseases associated with CGRP receptor)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 66 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:72404 CAPLUS Full-text
DN 145:159039
TI Validated ligand mapping of ACE active site
AU Kuster, Daniel J.; Marshall, Garland R.
CS Center for Computational Biology, Washington University, St. Louis, MO, 63110, USA
SO Journal of Computer-Aided Molecular Design (2006), 19(8), 609-615
CODEN: JCADEQ; ISSN: 0920-654X
PB Springer
DT Journal
LA English
AB Crystal structures of angiotensin-converting enzyme (ACE) complexed with three inhibitors (lisinopril, captopril, enalapril) provided exptl. data for testing the validity of a prior active site model predicting the bound conformation of the inhibitors. The ACE active site model - predicted over 18 years ago using a series of potent ACE inhibitors of diverse chemical structure - was recreated using published data and com. software. Comparison between the predicted structures of the three inhibitors bound to the active site of ACE and those determined exptl. yielded root mean square deviation (RMSD) values of 0.43-0.81 Å, among the distances defining the active site map. The bound conformations of the chemical relevant atoms were accurately deduced from the geometry of ligands, applying the assumption that the geometry of the active site groups responsible for binding and catalysis of amide hydrolysis was constrained. The mapping of bound inhibitors at the ACE active site was validated for known exptl. compds., so that the constrained conformational search methodol. may be applied with confidence when no exptl. determined structure of the enzyme yet exists, but potent, diverse inhibitors are available.

IT 107133-36-8, Aceon
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(angiotensin-converting enzyme active site model predicting conformation of bound inhibitors)

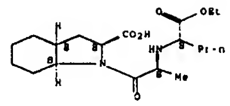
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

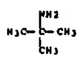
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 67 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1311320 CAPLUS Full-text
DN 144:7101
TI Method for synthesis of perindopril and its pharmaceutically acceptable salts
IN Fugier, Claude; Dubuffet, Thierry; Langlois, Pascal
PA Adir et Compagnie, Fr.; Les Laboratoires Servier
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1367063	A1	20031203	EP 2003-291931	20030731
	EP 1367063	B1	20060823		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 337332	T	20060915	AT 2003-291931	20030731
	ES 2271498	T3	20070416	ES 2003-3291931	20030731
	AU 2004261439	A1	20050210	AU 2004-261439	20040729
	CA 2533005	A1	20050210	CA 2004-2533005	20040729
	WO 2005012333	A2	20050210	WO 2004-FR2035	20040729
	WO 2005012333	A3	20050324		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

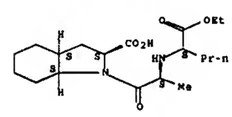
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1826352	A	20060830	CN 2004-80021209	20040729
	BR 2004013169	A	20061003	BR 2004-13169	20040729
	JP 2007526896	T	20070920	JP 2006-521621	20040729
	IN 2006DN00460	A	20070831	IN 2006-DN460	20060127
	MX 2006PA01243	A	20060411	MX 2006-PA1243	20060131
	US 2006183920	A1	20060817	US 2006-566562	20060131
	NO 2006000922	A	20060224	NO 2006-922	20060224
PRAI	EP 2003-291931	A	20030731		
	WO 2004-FR2035	W	20040729		

OS MARPAT 144:7101

AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH2Cl2-EtNPr-i2 at room temperature and MeCN-Et3N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).

IT 82834-16-0P 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

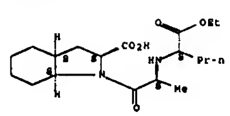


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

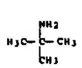
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



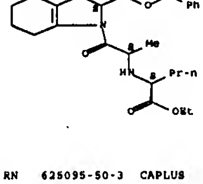
CM 2

CRN 75-64-9
CMF C4 H11 N



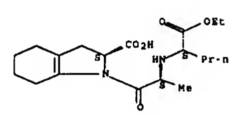
IT 539820-43-4P 625095-50-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)
RN 539820-43-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 625095-50-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 68 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1311047 CAPLUS Full-text
DN 144:7100
TI Method for synthesis of perindopril and its pharmaceutically acceptable salts
IN Fugier, Claude; Dubuffet, Thierry; Langlois, Pascal
PA Adir et Compagnie, Fr.; Les Laboratoires Servier
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1367062	A1	20031203	EP 2003-291930	20030731
	EP 1367062	B1	20060830		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 338058	T	20060915	AT 2003-291930	20030731
	ES 2271497	T3	20070416	ES 2003-3291930	20030731
	AU 2004261440	A1	20050210	AU 2004-261440	20040729
	WO 2005012328	A2	20050210	WO 2004-FR2036	20040729
	WO 2005012328	A3	20050324		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1826351	A	20060830	CN 2004-80021208	20040729
	JP 2006528653	T	20061221	JP 2006-521622	20040729
	IN 2006DN00468	A	20070831	IN 2006-DN468	20060127
	US 2006189813	A1	20060824	US 2006-566558	20060131
PRAI	EP 2003-291930	A	20030731		
	WO 2004-FR2036	W	20040729		

OS CASREACT 144:7100; MARPAT 144:7100

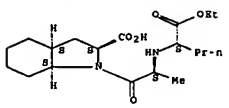
AB A method for the synthesis of perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] involves coupling of (2S)-hexahydroindole-2-carboxylic acid or its benzyl

ester with (R)-G-CHMeCOCl (G = Cl, Br, OH, tosyloxy, mesyloxy or trifluoromethanesulfonyloxy) and then (S)-Et 2-aminopentanoate, followed by catalytic hydrogenation. In an example, the resp. coupling reactions were carried in CH2Cl2-EtNPr-i2 at room temperature and MeCN-Et3N at reflux. Yield of perindopril following hydrogenation was 95% (enantiomeric purity 99%).

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

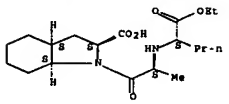


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

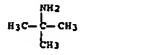
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

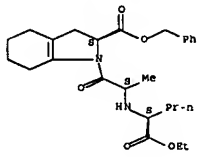
CRN 75-64-9
CMF C4 H11 N



IT 539820-43-4P 625095-50-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril from hexahydroindolecarboxylate and bromopropionyl chloride)

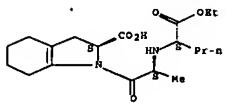
RN 539820-43-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 625095-50-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 69 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1290025 CAPLUS Full-text
DN 144:36329

TI Thiazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Cow, Christopher; Xie, Yongping; Wang, Xing; Russo, Ross; Azimioara, Mihai; Saez, Enrique
PA IRM LLC, Bermuda
SO PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005116000	A1	20051208	WO 2005-US18167	20050524
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005247931	A1	20051208	AU 2005-247931	20050524
CA 2563818	A1	20051208	CA 2005-2563818	20050524
EP 1748993	A1	20070207	EP 2005-754130	20050524
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1980906	A	20070613	CN 2005-80016538	20050524
US 2007203155	A1	20070830	US 2006-597282	20061121
KR 2007030791	A	20070316	KR 2006-724606	20061123
IN 2006CN04307	A	20070615	IN 2006-CN4307	20061123
NO 2006005984	A	20070705	NO 2006-5984	20061222
PRAI US 2004-574137P	P	20040524		
US 2005-648985P	P	20050131		
WO 2005-US18167	W	20050524		

OS MARPAT 144:36329
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

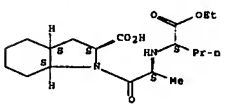
AB The invention relates to thiazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, p is 0-3; L is selected from -XOX-, -XS(O)mX-, and -XS(O)mXO-, where m is 0-2 and X is a bond or (un)substituted C1-4 alkylene; R1 is selected from halo, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl, C1-6 haloalkyl, C1-6 haloalkoxy, (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl, (un)substituted C3-12 cycloalkyl, and (un)substituted C3-8 heterocyclyl; R2 is -XOXCO2R5 or -XCO2R5, where X is as defined previously and R5 is H or C1-6 alkyl; and R3 and R4 are independently selected from R6 and R6Y, where R6 is (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl, and Y is selected from C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, -C(O)N(R5)-, and -OX-, where X and R5 are as defined previously, or R3 and R4, together with the atoms to which they are attached, form fused

bi- or tricyclic C5-14 heteroaryl, including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Cyclocondensation of 2-bromo-4'-methoxyacetophenone with thioacetamide followed by bromination, demethylation, and alkylation with iso-Pr iodide gave bromothiazole II, which was brominated and substituted with phenol III (preparation in 3 steps from 4-hydroxy-3-methylacetophenone given) to give thiazole IV. Compound IV underwent Suzuki coupling with 4-(trifluoromethoxy)phenylboronic acid and ester hydrolysis to give thiazole V. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of thiazole compds. as PPAR modulators and their use for treatment and prevention of diseases associated with PPARδ activity)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 70 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1289979 CAPLUS Full-text
DN 144:36326
TI Oxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Xie, Yongping; Wang, Xing; Cow, Christopher; Russo, Ross
PA IRM LLC, Bermuda
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005116016	A1	20051208	WO 2005-US18166	20050524
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,				

LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2005247930	A1	20051208	AU 2005-247930	20050524
CA 2563819	A1	20051208	CA 2005-2563819	20050524
EP 1749003	A1	20070207	EP 2005-775612	20050524
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1980919	A	20070613	CN 2005-80016511	20050524
KR 2007043705	A	20070425	KR 2006-724605	20061123
IN 2006CN04308	A	20070615	IN 2006-CN4308	20061123
NO 2006005983	A	20070205	NO 2006-5983	20061222
US 2007244130	A1	20071018	US 2007-597260	20070705
PRAI US 2004-574137P	P	20040524		
US 2005-649671P	P	20050202		
WO 2005-US18166	W	20050524		

OS MARPAT 144:36326

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

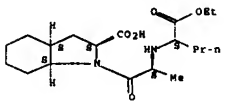
AB The invention relates to oxazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, p is 0-3; L is selected from -XOX-, -XS(O)mX-, and -XS(O)mXO-, where m is 0-2 and X is a bond or (un)substituted C1-4 alkylene; R1 is selected from halo, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl, C1-6 haloalkyl, C1-6 haloalkoxy, (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl, (un)substituted C3-12 cycloalkyl, and (un)substituted C3-8 heterocyclyl; R2 is -XOXCO2R5 or -XCO2R5, where X is as defined previously and R5 is H or C1-6 alkyl; and R3 and R4 are independently selected from R6 and R6Y, where R6 is (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl, and Y is selected from C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, -C(O)N(R5)-, and -OX-, where X and R5 are as defined previously, or R3 and R4, together with the atoms to which they are attached, form fused bi- or tricyclic C5-14 heteroaryl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Diastoization of 4-(trifluoromethoxy)acetophenone followed by heterocyclization with acetonitrile, and bromination gave bromooxazole II, which was brominated and substituted with phenol III (preparation in 3 steps from 4-hydroxy-3-methylacetophenone given) to give oxazole IV. Compound IV underwent Suzuki coupling with 2-isopropoxypyridin-5-ylboronic acid (preparation from 2-chloro-5-bromopyridine given) and ester hydrolysis to give oxazole V. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of oxazoles as PPAR modulators and their use for treatment and prevention of diseases associated with PPARδ activity)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L48 ANSWER 71 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:1262577 CAPLUS Full-text

DN 144:7098

TI Process for the preparation of perindopril and its salts

IN Meralavic, Marjon Sajid, Janja; Tomsic, Zdenka

PA Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia

SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005113500	A1	20051201	WO 2005-EP5048	20050510
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21800	A	20051231	SI 2004-143	20040514
SI 21852	A	20060228	SI 2004-235	20040805
AU 2005245087	A1	20051201	AU 2005-245087	20050510
CA 2566754	A1	20051201	CA 2005-2566754	20050510
EP 1753720	A1	20070221	EP 2005-748048	20050510
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA,				

HR, LV, MK, YU

NO 2006005695	A	20061211	NO 2006-5695	20061211
PRAI SI 2004-143	A	20040514		
SI 2004-235	A	20040805		
WO 2005-EP5048	W	20050510		

OS CASREACT 144:7098; MARPAT 144:7098

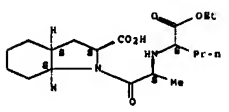
AB The invention relates to a process for the preparation of the ACE inhibitor perindopril, its pharmaceutically-acceptable salts and intermediates obtained in the process. The process involves conversion of N-[(1S)-1-carbethoxybutyl]-L-alanine to the acid chloride hydrochloride and reaction with (2S,3aS,7aS)-octahydroindole-2-carboxylic acid or a an ester or salt. The examples describe the synthesis of perindopril erbumine by reactions carried out in CH2Cl2.

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine 120465-02-3P 122454-52-8P 869877-96-3P 869954-04-1P 869954-08-5P 869954-09-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of perindopril and its salts)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



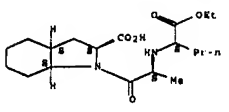
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



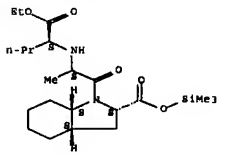
CM 2

CRN 75-64-9
CMF C4 H11 N

RN 120465-02-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, trimethylsilyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

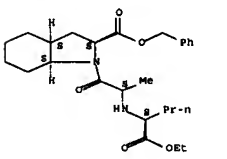
Absolute stereochemistry.



RN 122454-52-8 CAPLUS

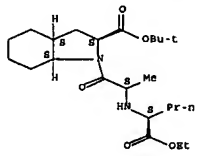
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



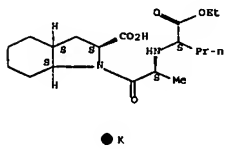
RN 869877-96-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 869954-04-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monopotassium salt, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

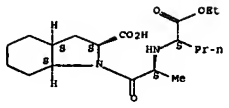
Absolute stereochemistry. Rotation (-).



● K

RN 869954-08-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monolithium salt, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

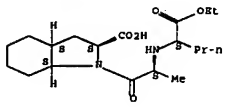
Absolute stereochemistry. Rotation (-).



● Li

RN 869954-09-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, sodium salt (1:1), (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● Na

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 72 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1262399 CAPLUS Full-text
DN 144:22712
TI Triaryl compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Azimioara, Mihai
PA Irm LLC, Bermuda
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005113506	A1	20051201	WO 2005-US16747	20050513
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,				

ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2005245418	A1	20051201	AU 2005-245418	20050513
	CA 2564365	A1	20051201	CA 2005-2564365	20050513
	EP 1756062	A1	20070228	EP 2005-751010	20050513
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 1980894	A	20070613	CN 2005-80019645	20050513
	BR 2005010024	A	20070925	BR 2005-10024	20050513
	IN 2006CN04198	A	20070615	IN 2006-CN4198	20061114
	US 2007259890	A1	20071108	US 2006-596598	20061114
PRAI	US 2004-571004P	P	20040514		
	WO 2005-US16747	W	20050513		
OS	MARPAT 144:22712				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

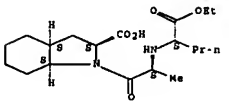
AB The invention relates to aryl compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, m is 0-3; X, Y, and Z are independently selected from CH and N; L is (un)substituted (CH2)nO(CH2)n or (CH2)nS(O)p(CH2)n, where each n is independently selected from 0-4 and p is 0-2; R1 and R2 are independently selected from (un)substituted C3-12 cycloalkyl-A-, (un)substituted C3-8 heterocyclyl-A-, (un)substituted C6-10 aryl-A-, and (un)substituted C5-13 heteroaryl-A-, where A is a bond, C1-6 alkylene, C2-6 alkenylene, or C2-6 alkynylene; R3 is selected from halo, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl, C1-6 haloalkyl, C1-6 haloalkoxy, (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl, (un)substituted C3-12 cycloalkyl, and (un)substituted C3-8 heterocyclyl; and R4 is selected from (CH2)nO(CH2)nCO2R5 and (CH2)nCO2R5, where n is as defined previously and R5 is H or C1-6 alkyl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Substitution of Me bromoacetate with 4-hydroxy-3-methylacetophenone followed by Baeyer-Villiger oxidation and methanolysis gave phenoxyacetate II, which underwent substitution of 3,5-dibromobenzyl bromide to give dibromobenzyl ether III. Treatment of III with an excess of 4-trifluoromethylphenylboronic acid and ester hydrolysis resulted in the formation of terphenyl IV. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of triaryl compds. as PPAR modulators and their use for treatment and prevention of diseases associated with PPARδ activity)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA

INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 73 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1259663 CAPLUS Full-text
DN 144:22911
TI Isoxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Russo, Ross; Azimioara, Mihai; Xie, Yongping
PA IRM LLC, Bermuda
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005113519	A1	20051201	WO 2005-US16672	20050512
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005245411	A1	20051201	AU 2005-245411	20050512
	CA 2564429	A1	20051201	CA 2005-2564429	20050512
	EP 1745027	A1	20070124	EP 2005-769154	20050512
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 1984894	A	20070620	CN 2005-80019652	20050512
	KR 2007034993	A	20070329	KR 2006-723769	20061113
	IN 2006CN04201	A	20070622	IN 2006-CN4201	20061114
PRAI	US 2004-571003P	P	20040514		
	WO 2005-US16672	W	20050512		
OS	MARPAT 144:22911				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

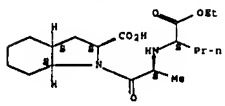
AB The invention relates to isoxazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, R1 is selected from (un)substituted C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; R2 is selected from (CH2)nO(CH2)nOR5, (CH2)nOR5, CO2R5, C(O)N(R4)2, C(O)N(R4)(CH2)nOR4, CO2(CH2)nOR5, C(O)(CH2)nOR5, C(O)N(R4)(CH2)nOR5, C(O)N(R4)(R5), and C(O)N(R4)(CH2)nR5, where n is 0-4, R4 is H or C1-6 alkyl, and R5 is C1-6 alkyl, C3-12 cycloalkyl, C3-8 heterocyclyl, C6-10 aryl, or C5-10 heteroaryl, or R4 and R5, together with the nitrogen atom to which they are attached, form C3-8 heterocyclyl or C5-10 heteroaryl; and R3 is selected from (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the uses of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Esterification of 3-bromophenylacetic acid followed by coupling with cyanide, reduction of the nitrile to an aldehyde, condensation with hydroxylamine, and chlorination gave chlorooxime II. N-Boc-2-bromoethylamine was substituted with 2,4-dichlorophenol followed by deprotection, amidation with Et benzoylacetate to give benzoylacetamide III, which underwent cyclocondensation with chlorooxime II and ester hydrolysis, resulting in the formation of isoxazole IV. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. and compns. as PPAR modulators and their use for treatment and prevention of diseases associated with activity of PPAR families, particularly PPARδ)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 74 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:1201076 CAPLUS Full-text
DN 143:446810
TI Processes for the preparation of alpha polymorph of perindopril erbumine
IN Joshi, Narendra Shriram; Bhirud, Shekhar Bhaskar; Rao, Kodali Eswara
PA Glenmark Pharmaceuticals Limited, India
SO U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005250706	A1	20051110	US 2005-122731	20050505
WO 2005108365	A1	20051117	WO 2005-IB1233	20050506

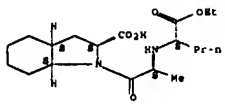
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI IN 2004-MU531 A 20040507
US 2004-572402P P 20040519
OS MARPAT 143:446810
AB A process for the preparation of an alpha polymorph of perindopril erbumine is provided comprising (a) forming a solution comprising perindopril erbumine in one or more ketones; (b) heating the solution to reflux; and (c) cooling the solution to a temperature sufficient to form the alpha polymorph of perindopril erbumine. The alpha polymorphs of perindopril erbumine obtained herein have a high purity level.
IT 107133-36-8P, Perindopril erbumine
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(of perindopril erbumine α-polymorph)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L8 ANSWER 75 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1177978 CAPLUS Full-text
DN 143:446753
TI Pharmaceutical aerosol composition containing poorly water-soluble active agent, a non-ionic surfactant, and a phospholipid
IN Jauernig, Jurgen; Lintz, Frank-Christophe; Keller, Manfred; Friedrich, Ingo
PA Pari G.m.b.H., Germany
SO U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of Appl. No. PCT/EP04/011571.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

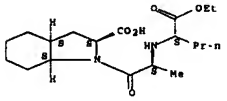
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005244339	A1	20051103	US 2005-106999	20050414
DE 10347994	A1	20050616	DE 2003-10347994	20031015
WO 2005037246	A2	20050428	WO 2004-EP11571	20041014
WO 2005037246	A3	20051208		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI DE 2003-10347994 A 20031015
WO 2004-EP11571 A2 20041014

AB Sterile compns. for administration as aerosols are described. They contain an active agent which is poorly water-soluble, a non-ionic surfactant a component and a phospholipid component. The compns. are suitable for oral or nasal inhalation, but also for topical or or mucosal administration. They are particularly useful for the efficient pulmonary administration of poorly soluble corticosteroids and can be aerosolized with common nebulizers. A colloidal solution contained cyclosporin 0.06, Tyloxapol 1.0, dimyristoyl phosphatidyl choline 1.0, propylene glycol 1.0, sodium chloride 0.7, and water for injection q.s. 100 mL. The average particle size of this colloidal solution was 9.7 nm.
IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical aerosol composition)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 76 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1146100 CAPLUS Full-text
DN 143:420385
TI Development of efficient genotyping method for detecting insertion/deletion type polymorphisms of human angiotensin converting enzyme gene
IN Katsuragi, Tomohiro; Sugimoto, Ken; Akasaka, Tadashi; Ogiwara, Toshio
PA EBS K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2005295938	A	20051027	JP 2004-119417	20040414
PRAI JP 2004-119417		20040414		

AB An efficient genotyping method for detecting insertion/deletion type polymorphism of human angiotensin converting enzyme gene. The method is designed to detect the polymorphisms in the extracted genomic DNA samples by the real time PCR using the specifically designed primers and probes with fluorometric (FRET) detection. The ACE gene polymorphism anal. is especially established for diagnostic prediction of the genetic susceptibility to cardiac infarction, cardiac hypertrophy, diabetic nephropathy, IgA nephropathy or purpura nephritis. The ACE genotypes are classified into the DD, ID and II types and the order of the susceptibility to the above mentioned diseases is DD > ID > II. The genotyping method is also applied to predict the

effectiveness of the ACE inhibitors in the therapy of hypertension. The order of the effectiveness of the ACE inhibitors is DD > ID > II. The ACE inhibitors that can be subjected to this effectiveness prediction test are alacepril, imidapril hydrochloride, quinapril hydrochloride, temocapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, captopril, trandolapril, perindopril erbumine, enalapril maleate, lisinopril, lactotripeptide and the peptides from dried bonito or sardine.

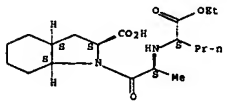
IT 107133-36-8, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effectiveness dependent on genotype; development of efficient genotyping method for detecting insertion/deletion type polymorphisms of human angiotensin converting enzyme gene)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L8 ANSWER 77 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1123812 CAPLUS Full-text
DN 143:379815
TI Method of reducing C-reactive protein using growth hormone secretagogues
IN Polvino, William J.; Carpi, David B.; Smith, Roy G.
PA Rejuvenon Corporation, USA
SO PCT Int. Appl., 135 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

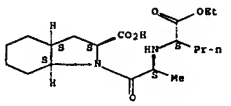
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005097261	A1	20051020	WO 2005-US10927	20050330
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2565324	A1	20051020	CA 2005-2565324	20050330
	US 2005261201	A1	20051124	US 2005-94339	20050330
	EP 1735055	A1	20061227	EP 2005-733103	20050330
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	JP 2007531769	T	20071108	JP 2007-506567	20050330
	KR 2007010151	A	20070122	KR 2006-721482	20061017
PRAI	US 2004-557466P	P	20040330		
	WO 2005-US10927	W	20050330		

OS MARPAT 143:379815
AB The invention discloses a method for reducing C-reactive protein in a subject in need of treatment thereof, wherein the subject is at risk of having or the subject has already had a vascular event or suffering from an inflammatory disease or disorder. In one embodiment, the vascular event is a cardiovascular event (e.g., myocardial infarction). In another embodiment, the vascular event is a cerebrovascular event (e.g., stroke, transient ischemic attacks). In yet another embodiment the vascular event is a peripheral vascular event (e.g., intermittent claudication). The method comprises administering a therapeutically effective amount of at least one growth hormone secretagogue compound or a pharmaceutically acceptable salt, hydrate or solvate thereof. The growth hormone secretagogue can be coadministered with a second growth hormone secretagogue, HMG CoA reductase inhibitor, an ACAT inhibitor, a CETP inhibitor, an anti-inflammatory agent, an ACE inhibitor, a Beta blocker, a cholesterol absorption inhibitor, a nicotonic acid, a fabric acid derivative, a bile acid sequestering agent or a combination thereof.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(growth hormone secretagogues for reducing C-reactive protein, and use with other agents)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 78 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1117891 CAPLUS Full-text
DN 143:367597
TI Process for the preparation of perindopril
IN Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PA Neopharma Limited, UK
SO Brit. UK Pat. Appl., 21 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2413128	A	20051019	GB 2004-8258	20040413
	AU 2005232938	A1	20051027	AU 2005-232938	20050407
	CA 2562843	A1	20051027	CA 2005-2562843	20050407
	WO 2005100317	A1	20051027	WO 2005-GB1355	20050407
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1751107	A1	20070214	EP 2005-732439	20050407
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	JP 2007532616	T	20071115	JP 2007-507836	20050407
	IN 2006DN06462	A	20070831	IN 2006-DN6462	20061101
	KR 2007054142	A	20070528	KR 2006-723684	20061113
	US 2007185335	A1	20070809	US 2007-599918	20070409
PRAI	GB 2004-8258	A	20040413		
	WO 2005-GB1355	W	20050407		

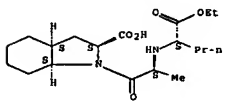
OS CASREACT 143:367597; MARPAT 143:367597
AB A process for preparing perindopril or a pharmaceutically-acceptable salt comprises coupling a 4-halo-, 4-alkoxy- or 4-nitrobenzyl ester of (2S,3aS,7aS)-2-carboxyoctahydroindole with N-[(S)-1-carbethoxybutyl]-L-alanine (1) in the presence of DCC and HOBT, followed by catalytic hydrolgenolysis. The starting ester was obtained from (S)-indoline-2-carboxylic acid by hydrogenation-esterification and 1 was obtained from

norvaline Et ester and pyruvic acid under catalytic hydrogenation conditions. The method was applied to the synthesis perindopril erbumine (20.5 g obtained from 24 g 4-chlorobenzyl ester and 21.26 g 1).

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril by acylation of octahydroindolecarboxylates with ethoxycarbonylbutylalanine)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

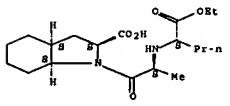


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

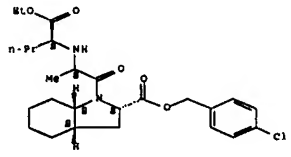


CM 2

CRN 75-64-9
CMF C4 H11 N

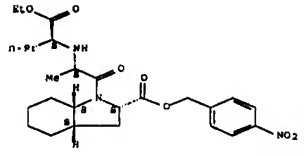
IT [illegible] OR 866430-96-8
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril by acylation of octahydroindolecarboxylate with ethoxycarbonylbutylalanine)
RN 793716-56-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (4-chlorophenyl)methyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 866430-96-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (4-nitrophenyl)methyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

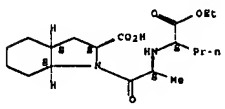


RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 79 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1107718 CAPLUS Full-text
DN 144:148257
TI Role of transforming growth factor-β2 in, and a possible Transforming growth factor-β2 gene polymorphism as a marker of, renal dysfunction in essential hypertension: A study in turkish patients
AU Bicik, Zerrin; Gonen, Sevim; Bahcebasi, Talat; Reis, Kadriye; Arinsoy, Turgay; Sindel, Sukru
CS Department of Nephrology, Medical Faculty, Abant Izzet Baysal University, Duzce, Turk.
SO Current Therapeutic Research (2005), 66(4), 266-278
CODEN: CTCRA9; ISSN: 0011-393X
PB Excerpta Medica, Inc.
DT Journal
LA English
AB Background: Many studies have shown that transforming growth factor (TGF)-β has a major role in renal scarring in many renal diseases and hypertension. Objectives: The primary aim of this study was to investigate both the relationship between hypertension and serum and urinary levels of TGF-β2 (a more sensitive isoform for glomeruli than TGF-β1), and the effects of combination therapy with perindopril + indapamide on microalbuminuria, which becomes an early indicator of hypertensive benign nephropathy, and serum and urinary TGF-β2 levels in patients with mild to moderate essential hypertension. In addition, we examined the possible relationship between TGF-β2 gene polymorphism and essential hypertension. Methods: This study was conducted at the Department of Nephrol., Medical Faculty, Gazi University, Ankara, Turkey. Patients aged ≥18 years with newly diagnosed mild to moderate essential hypertension (systolic/diastolic blood pressure [SBP/DBP] >120/>80 mm Hg) who had not previously received antihypertensive treatment were included in the study. Patients with stage I hypertension received perindopril 2 mg + indapamide 0.625 mg (tablet), and patients with stage II hypertension received perindopril 4 mg + indapamide 1.125 mg (tablet). All study drugs were given OD (morning) PO with food for 6 mo. Serum and urinary TGF-β2 and creatinine levels and serum and urinary albumin levels were measured before and after perindopril + indapamide administration. Amplified DNA fragments of the TGF-β2 primer region were screened using amplification refractory mutation system polymerase chain reaction anal., and the number of ACA repeats was confirmed by DNA sequencing. Genetic studies were performed using a com. TGF-β2 kit. Results: Forty patients were enrolled in the study, and 38 patients (27 women, 11 men; mean [SD] age, 46.3 [6.5] years) completed it. SBP and DBP were significantly decreased from baseline with perindopril/indapamide (both, $P < 0.001$). Microalbuminuria and urinary TGF-β2 levels also decreased significantly from baseline ($P = 0.04$ and $P < 0.001$, resp.), whereas the serum TGF-β2 level did not change significantly. Three patients, all of whom were found to have TGF-β2 gene mutations, had increased urinary TGF-β2 levels despite good blood pressure control. Conclusions: The results of this study in patients with mild to moderate hypertension suggest that, despite good clin. control of blood pressure, the persistence of microalbuminuria and high urinary TGF-β2 levels might predict renal impairment. When treating these patients, genetic tendencies and possible polymorphisms on the TGF-β2 locus should be kept in mind.
IT 82834-16-0, Perindopril
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined therapy of perindopril and indapamide reduced SBP and DBP, reduced microalbuminuria and urinary TGF-β2 but not of serum and

TGF-β2 gene mutation was associated with higher urinary TGF-β2 level in hypertensive patient)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

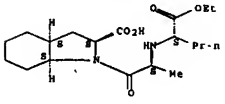
L8 ANSWER 80 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:962026 CAPLUS Full-text
DN 143:254016
TI Combination of (S)-amlodipine and an ACE inhibitor for reducing hypertension
IN Bush, Larry; Grogan, Donna Roy
PA Sepracor Inc., USA
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005079772	A2	20050901	WO 2005-US4460	20050214
WO 2005079772	A3	20051103		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI US 2004-545451P	P	20040218		
US 2004-554030P	P	20040316		
US 2005-649635P	P	20050203		

AB The present invention generally relates to pharmaceutical compns. comprising optically pure (S)-amlodipine and an ACE inhibitor. In a preferred embodiment the (S)-amlodipine is (S)-amlodipine-L-malate, or a polymorph, pseudopolymorph or solvate thereof. In a preferred embodiment, the ACE inhibitor is ramipril. The pharmaceutical compns. of the invention are useful in the treatment of hypertension. The present invention also relates to a method of treating a

patient suffering from hypertension or a cardiac disorder, comprising co-administering a therapeutically effective amount of optically pure (S)-amlodipine and an ACE inhibitor. In a preferred embodiment the (S)-amlodipine is (S)-amlodipine-L-malate, or a polymorph, pseudopolymorph or solvate thereof. In a preferred embodiment, the ACE inhibitor is ramipril. The preparation and properties of (S)-amlodipine L-malate solvates and the polymorphs are given.
IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of amlodipine and ACE inhibitor for reducing hypertension)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 81 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:729537 CAPLUS Full-text
DN 143:211920
TI Preparation of diacylglycerol acyltransferase (DGAT1) inhibitors as anorectics.
IN Ogawa, Nobuya; Okuma, Chihiro; Furukawa, Noboru
PA Japan Tobacco Inc., Japan; Amgen Sf, LLC
SO PCT Int. Appl., [illegible] pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

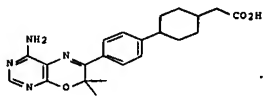
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005072740	A2	20050811	WO 2005-JP1643	20050128
WO 2005072740	A3	20051027		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005209115	A1	20050811	AU 2005-209115	20050128
CA 2554455	A1	20050811	CA 2005-2554455	20050128
EP 1718309	A2	20061108	EP 2005-704403	20050128

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

CN 1913899	A	20070214	CN 2005-80003524	20050128
JP 2007519605	T	20070719	JP 2006-524132	20050128
US 2007027093	A1	20070201	US 2006-495095	20060728
IN 2006CN03150	A	20070608	IN 2006-CN3150	20060830
PRAI JP 2004-24812	A	20040130		
US 2004-598037P	P	20040802		
WO 2005-JP1643	W	20050128		

OS CASREACT 143:211920; MARPAT 143:211920

GI



I

AB Claimed are anorectics comprising as active ingredients compds. having DGAT inhibitory activity (DGAT1 inhibitory activity) or a prodrugs or a pharmaceutically acceptable salts thereof. Thus, title compound (I) (preparation given) at 10 mg/kg orally in rats gave a 30% reduction in food consumption after 8 h.

IT 107133-36-8, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of diacylglycerol acyltransferase (DGAT1) inhibitors as anorectics)

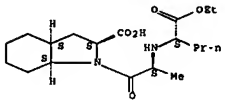
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

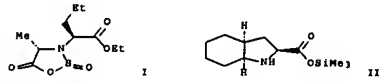
CRN 75-64-9
CMF C4 H11 N

L8 ANSWER 82 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:698368 CAPLUS Full-text
DN 143:173145
TI Preparation of perindopril
IN Bhirud, Shekhar Bhaskar; Ahmed, Suhail; Chandrasekhar, Batchu; Purushotham, Vandanapu Loka Appala
PA India
SO U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005171165	A1	20050804	US 2004-985097	20041110
PRAI IN 2003-MU1179	A	20031112		
US 2004-569041P	P	20040507		

OS CASREACT 143:173145

GI



I II

AB A process for preparing a novel intermediate, oxathiazolidinedione I, in the preparation of perindopril is provided. Thus, reacting thionyl chloride in CH2Cl2 with imidazole and N-1(S)-(carboxyethyl)butyl-(S)-alanine gave I. Also provided are improved processes for the preparation of perindopril erbumine comprising (a) reacting I with a silylated octahydroindole-1H-2- carboxylic acid II to form perindopril; and (b) reacting perindopril with tert-butylamine to form perindopril erbumine.

IT 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril and perindopril erbumine)

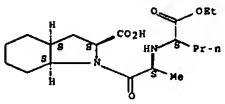
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

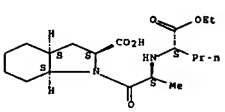
CRN 75-64-9
CMF C4 H11 N

IT 82834-16-0P, Perindopril
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril and perindopril erbumine)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 83 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:673315 CAPLUS Full-text
DN 143:159626
TI Inclusion complexes of perindopril
IN Rucman, Rudolf
PA LEK Pharmaceuticals D.D., Slovenia
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005068490	A1	20050728	WO 2005-EP282	20050113
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21703	A	20050831	SI 2004-11	20040114
EP 1709066	A1	20061011	EP 2005-700892	20050113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
PRAI SI 2004-11	A	20040114		
WO 2005-EP282	W	20050113		

AB Complexes of the ACE-inhibitor perindopril, a salt, an addition salt or a derivative thereof with cyclodextrins, polyvinylpyrrolidone or hydroxypropyl cellulose, and processes for their preparation are described. E.g., complexes of perindopril erbumine with β-cyclodextrin and Me and hydroxypropyl β-cyclodextrins were prepared

IT 107133-36-8DP, Perindopril erbumine, compds., with hydroxypropyl and Me cyclodextrins 860260-85-1P 860260-86-2P 860260-87-3P 860260-88-4P 860260-89-5P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inclusion complexes of perindopril)

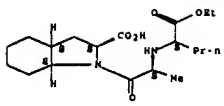
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

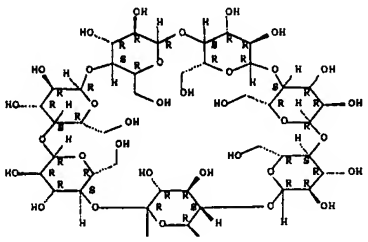
RN 860260-85-1 CAPLUS
CN β-Cyclodextrin, compd. with 2-methyl-2-propanamine (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 7585-39-9
CMF C42 H70 O35

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

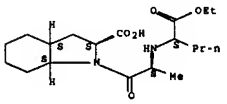
CM 2

CRN 107133-36-8
CMF C19 H32 N2 O5 . C4 H11 N

CM 3

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 4

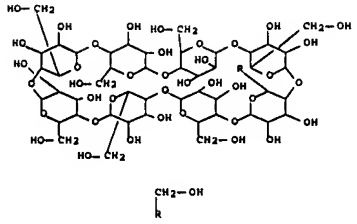
CRN 75-64-9
CMF C4 H11 N

RN 860260-86-2 CAPLUS
CN γ-Cyclodextrin, compd. with 2-methyl-2-propanamine (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 17465-86-0

CMF C48 H80 O40



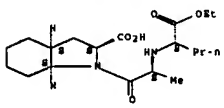
CM 2

CRN 107133-36-8
CMF C19 H32 N2 O5 . C4 H11 N

CM 3

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 4

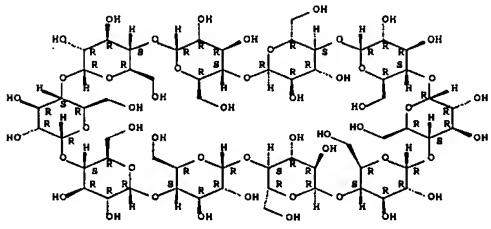
CRN 75-64-9
CMF C4 H11 N

RN 860260-87-3 CAPLUS
CN ε-Cyclodextrin, compd. with 2-methyl-2-propanamine (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (9CI) (CA INDEX NAME)

CM 1

CRN 156510-98-4
CMF C60 H100 O50

Absolute stereochemistry.



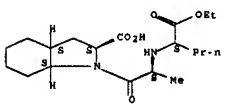
CM 2

CRN 107133-36-8
CMF C19 H32 N2 O5 . C4 H11 N

CM 3

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 4

CRN 75-64-9
CMF C4 H11 N

RN 860260-88-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 1-ethenyl-2-pyrrolidinone homopolymer and 2-methyl-2-propanamine (1:7:1) (9CI) (CA INDEX NAME)

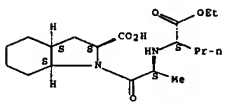
CM 1

CRN 107133-36-8
CMF C19 H32 N2 O5 . C4 H11 N

CM 2

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 3

CRN 75-64-9
CMF C4 H11 N

CM 4

CRN 9003-39-8
CMF (C6 H9 N O)x
CCI PMS

CM 5

CRN 88-12-0
CMF C6 H9 N O

RN 860260-89-5 CAPLUS
CN Cellulose, 2-hydroxypropyl ether, compd. with (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid and 2-methyl-2-propanamine (?:1:1) (9CI) (CA INDEX NAME)

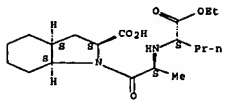
CM 1

CRN 107133-36-8
CMF C19 H32 N2 O5 . C4 H11 N

CM 2

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 3

CRN 75-64-9
CMF C4 H11 N

CM 4

CRN 9004-64-2
CMF C3 H8 O2 . x Unspecified

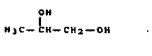
CM 5

CRN 9004-34-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

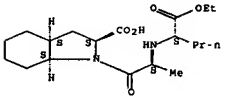
CM 6

CRN 57-55-6
CMF C3 H8 O2



IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(inclusion complexes of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



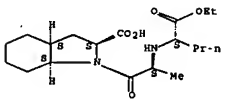
IT 107133-36-8, Perindopril erbumine
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(inclusion complexes of perindopril)

RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 84 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:673261 CAPLUS Full-text
DN 143:153713
TI New crystalline form of perindopril
IN Rucman, Rudolf
PA Lek Pharmaceuticals D. D., Slovenia
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

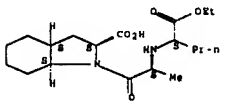
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005068425	A1	20050728	WO 2005-EP283	20050113

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

SI 21704 A 20050831 SI 2004-12 20040114
EP 1713771 A1 20061025 EP 2005-700893 20050113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU
PRAI SI 2004-12 A 20040114
WO 2005-EP283 W 20050113
OS CASREACT 143:153713
AB The invention relates to a process for the preparation of ACE inhibitor perindopril which starts from N-[(S)-1-carbethoxybutyl]-L-alanine and involves trimethylsilyl protection and conversion to reactive acid chloride for reaction with (2S,3aS,7aS)-octahydroindole-2-carboxylic acid having a protected carboxyl group. The invention also relates to new crystalline and amorphous forms of perindopril. Thus, perindopril obtained by reaction of silylated reactants was purified by filtering a CH2Cl2 solution through a silica gel column and crystallizing from an Et ether solution Perindopril in new crystalline form (78.2%) was obtained.
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crystal structure; preparation of perindopril in new crystalline form)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



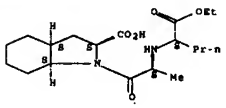
IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril in new crystalline form)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

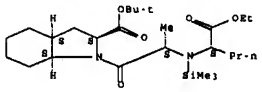


CM 2

CRN 75-64-9
CMF C4 H11 N

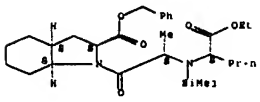
IT 859511-85-6P 861818-61-3P 861818-65-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril in new crystalline form)
RN 859511-85-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl](trimethylsilyl)amino]-1-oxopropyl]octahydro-, 1,1-dimethylethyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



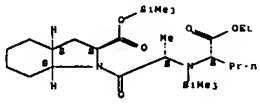
RN 861818-61-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl](trimethylsilyl)amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 861818-65-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl](trimethylsilyl)amino]-1-oxopropyl]octahydro-, trimethylsilyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

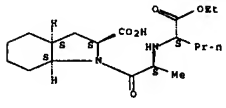


RE.CNT THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 85 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:616251 CAPLUS Full-text
DN 143:209860
TI Effect of genetic variation on therapy with angiotensin converting enzyme inhibitors or angiotensin receptor blockers in dialysis patients
AU Boeger, C. A.; Goetz, A. K.; Krueger, B.; Hoesl, M.; Schmitz, G.; Riegger, G. A. J.; Kraemer, B. K.
CS Klinik und Poliklinik fuer Innere Medizin II, University of Regensburg, Regensburg, Germany
SO European Journal of Medical Research (2005), 10(4), 161-168
CODEN: EJMREL; ISSN: 0949-2321
PB I. Holzapfel Verlag GmbH
DT Journal
LA English
AB Introduction: The role of interaction of polymorphisms in the Renin-Angiotensin-System (RAS) with angiotensin converting enzyme (ACE) or angiotensin receptor (AGTR1) inhibitors (RAS inhibitors) is unknown, as is the role of such therapy in end stage renal disease (ESRD) patients. Methods: We enrolled all 445 prevalent patients with diabetic nephropathy receiving maintenance hemodialysis in 30 centers in Southern Germany from August 1999 to Jan. 2000 for prospective survival anal. until Dec. 2003. Blood pressure and medication was recorded at inclusion. We determined survival specific for allelic variants of the ACE (insertion/deletion), Angiotensinogen (M235T) and AGTR1 (A1166C) genes. The effect of therapy with RAS inhibitors at study inclusion was determined for the allelic variants of each gene. The primary end point was all cause mortality (ACM). Results: For all polymorphisms, and for therapy with RAS inhibitors there was no significant effect on survival in

the complete collective (n = 445), though there was an insignificant trend for improved survival in patients on AGTR1 antagonists. Increased ACM risk was associated with treatment with RAS inhibitors only in patients homozygous for the wild type AGTR1 1166A allele (HR 1.65, p=0.01). For all other polymorphisms, therapy with RAS inhibitors had no significant effect on ACM, irresp. of genotype. Similar results were obtained in patients with systolic ventricular dysfunction. Conclusion: Our data do not show a survival advantage for type 2 diabetes hemodialysis patients receiving RAS inhibiting therapy. In addition, our data indicate that allelic variation in RAS genes and pharmacogenetic interaction with RAS inhibition does not affect mortality risk in diabetic hemodialysis patients.
IT 82834-16-0, Perindopril
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(RAS inhibiting therapy with ACE inhibitors perindopril did not improve survival of diabetic nephropathy patient receiving maintenance hemodialysis)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 86 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:436413 CAPLUS Full-text
DN 143:139085
TI Method for preparing N-carboxyalkyl dipeptide type angiotensin converting enzyme inhibitor
IN Shi, Huilin; Zhang, Qingwen; Zhong, Jingfen; Shan, Xiaoyan; Chen, Guoliang; Zhou, Minghua
PA Shanghai Research Institute of Pharmaceutical Industry, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 11 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1429835	A	20030716	CN 2002-139936	20021230
PRAI CN 2002-139936		20021230		

AB The dipeptide, (I, R3OCO-CHR1NHCHR2CONR4R5 wherein R1 = Pr or phenethyl; R2 = Me, 4-trifluoroacetamidobutyl, or 4-aminobutyl; and R3 = H or ethyl), is prepared by allowing to react R3OCOCHR1NHCHR2COOH with bis(trichloromethyl) carbonate in solvent at (-20)-100°C for 1-50 h to obtain N-carboxylic

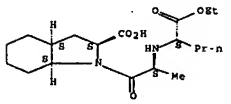
anhydride and then coupling with alpha-amino acid or its derivative in organic solvent at (-20)-100°C for 1-50 h. The alpha-amino acid or its derivative, R4R5NH, is 1,2,3,4-tetrahydro-3- isoquinolinecarboxylic acid benzyl ester, 2-azabicyclo[3.3.0]octane-3- carboxylic acid, 2-pyrrolidinecarboxylic acid, or octahydro-1H-indole-2- carboxylic acid.

IT 82834-16-0P, Perindopril
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tert-butylamine salt; method for preparing N-carboxyalkyl dipeptide type angiotensin converting enzyme inhibitor)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 87 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:412617 CAPLUS Full-text
DN 143:90592
TI Insertion/deletion polymorphism of the ACE gene and adherence to ACE inhibitors
AU Schelleman, H.; Klungel, O. H.; van Duijn, C. M.; Witteman, J. C. M.; Hofman, A.; de Boer, A.; Stricker, B. H. Ch
CS Department of Epidemiology & Biostatistics, Erasmus MC, Rotterdam, Neth.
SO British Journal of Clinical Pharmacology (2005), 59(4), 483-485
CODEN: BCPHBM; ISSN: 0306-5251
PB Blackwell Publishing Ltd.
DT Journal
LA English

AB We investigated whether the insertion/deletion (I/D) polymorphism of the ACE gene modified the adherence to ACE inhibitors as measured by the discontinuation of an ACE inhibitor, or addition of another antihypertensive drug. This was a cohort study among 239 subjects who started ACE inhibitor therapy. A Cox proportional hazard model was used to calculate relative risk (RR). During follow-up there was no significant difference between subjects with the DD, ID or II genotype (DD vs II; RR = 1.17, 95%CI: 0.78, 1.77 and ID vs II; RR = 1.06, 95%CI: 0.73, 1.55) in adherence. The I/D polymorphism of the ACE gene does not influence the adherence to ACE inhibitors.

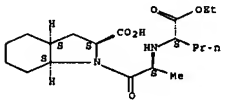
IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE gene insertion/deletion polymorphism and adherence to ACE inhibitors)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



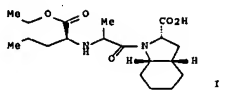
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

INSTANT

L8 ANSWER 88 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:371219 CAPLUS Full-text
DN 142:435775
TI Novel method for preparation of crystalline perindopril erbumine
IN Singh, Girij Pal; Godbole, Himanshu Madhav; Nehate, Sagar Purushottam
PA Lupin Ltd., India
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005037788	A1	20050428	WO 2003-IN340	20031021
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003300689	A1	20050505	AU 2003-300689	20031021
EP 1675827	A1	20060705	EP 2003-818870	20031021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003018561	A	20061010	BR 2003-18561	20031021
JP 2007518668	T	20070712	JP 2005-509586	20031021
US 2007149604	A1	20070628	US 2006-576386	20060419
IN 2006MN00495	A	20070824	IN 2006-MN495	20060427
PRAI WO 2003-IN340	A	20031021		

GI



I

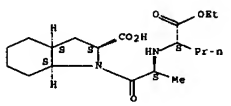
AB Crystalline perindopril erbumine (I.H2NBu-tert) is prepared and the x-ray (powder) diffraction pattern given. The process comprises reacting a solution of perindopril (I), in a solvent selected from DMF or di-Me acetals of lower aliphatic aldehydes and ketones with tertiary butylamine and crystallization of the erbumine salt thus obtained by heating the reaction mixture to reflux, filtering hot, cooling gradually to 20-30°, and further cooling to 0-15° for 30 min-1 h and finally filtering off and drying the crystals.

IT 82834-16-0P, Perindopril
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of crystalline perindopril erbumine)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 107133-36-8P, Perindopril erbumine
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of crystalline perindopril erbumine)

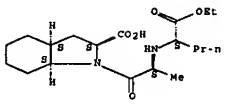
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

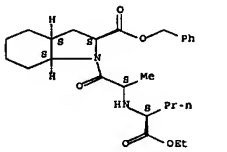
CRN 75-64-9
CMF C4 H11 N

IT 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of crystalline perindopril erbumine)

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 89 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:295060 CAPLUS Full-text
DN 143:90536
TI Mortality in patients with hypertension on angiotensin-I converting enzyme

(ACE)-inhibitor treatment is influenced by the ACE insertion/deletion polymorphism

AU Bleumink, Gysels S.; Schut, Anna F. C.; Sturkenboom, Miriam C. J. M.; Van Duijn, Cornelia M.; Deckers, Jaap W.; Hofman, Albert; Kingma, J. Herre; Witteman, Jacqueline C. M.; Stricker, Bruno H. Ch.

CS Department of Epidemiology & Biostatistics, Erasmus Medical Center, Rotterdam, 3000 DR, Neth.

SO Pharmacogenetics and Genomics (2005), 15(2), 75-81
CODEN: PGHEAI

PB Lippincott Williams & Wilkins

DT Journal

LA English

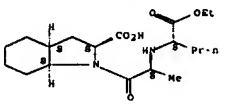
AB The response to angiotensin-I converting enzyme (ACE)-inhibitor therapy is highly variable. Residual ACE activity during treatment, potentially modified by the ACE insertion/deletion (I/D) polymorphism, may explain part of this variability. We studied the possible interaction between ACE-inhibitor therapy in patients with hypertension and the ACE I/D polymorphism in incident heart failure and death. We studied 3365 hypertensive participants of the population-based Rotterdam Study, without heart failure at baseline for whom ACE-genotyping was successful. Incident heart failure was defined according to established criteria. In addition, total and cardiovascular mortality were studied as endpoints. A Cox regression model with use of ACE-inhibitors defined as time-dependent covariates was used for data-anal. Interaction was tested in this model assuming an allele-effect relationship. Although we could not demonstrate a beneficial effect of ACE-inhibitors, there was significant interaction between the ACE I/D polymorphism (II-ID-DD) and ACE-inhibitor use in the prediction of total and cardiovascular mortality. Mortality risk associated with treatment increased with the number of D alleles present; e.g. for total mortality in the II genotype group: RR=0.95 (95% CI 0.63-1.45), in the ID genotype group: RR=1.08 (95% CI 0.84-1.38) and in the DD genotype group: RR=1.61 (95% CI 1.18-2.18). No statistically significant interaction was found for incident heart failure. The results of our study suggest a relative resistance to ACE-inhibitor therapy in subjects with hypertension and the DD genotype compared to the II genotype, with the ID genotype in an intermediate position.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE insertion/deletion influences mortality in hypertensive patients on ACE inhibitors)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 90 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:216790 CAPLUS Full-text

DN 142:298121

TI Preparation of biphenyl or phenylheterocyclyl moiety-containing esters as inhibitors of microsomal triglyceride transfer protein

IN Hagiwara, Atsushi; Ikenogami, Taku; Mera, Yasuko; Sumida, Yukako; Iida, Akio; Tadauchi, Toshio; Takahashi, Mitsuru

PA Japan Tobacco Inc., Japan

SO PCT Int. Appl., 229 pp.
CODEN: PIXXD2

DT Patent

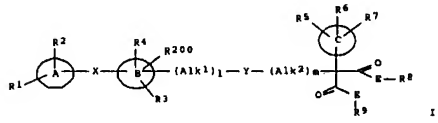
LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005021486	A1	20050310	WO 2004-JP12407	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1669345	A1	20060614	EP 2004-772363	20040827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2006205726	A1	20060914	US 2006-362375	20060227
PRAI JP 2003-305877	A	20030829		
WO 2004-JP12407	W	20040827		

OS MARPAT 142:298121

GI



AB The title compds. I [R1, R2 = H, alkyl, etc.; ring A = aryl, etc.; X = CO2(CH2)n, etc.; n = 0 - 3; R3, R4, R200 = H, halo, etc.; ring B = phenylene, etc.; ring C = Ph, etc.; R5, R6, R7 = H, alkyl, etc.; R8, R9 = H, (un)substituted alkyl, etc.; E = O, etc.; Y = OCO, etc.; Alk1, Alk2 = alkanediyl, etc.; l, m = 0 - 3] are prepared Thus, di-Et 2-(2-[3-acetoxy-4-

[(4'-trifluoromethylbiphenyl-2- carbonyl)amino]phenyl]acetoxymethyl)-2-phenylmalonate was prepared in 2 steps from di-Et 2-(2-(3-benzyloxy-4-[(4'-trifluoromethylbiphenyl-2- carbonyl)amino]phenyl]acetoxymethyl)-2-phenylmalonate. In a test for the inhibition of triglyceride transfer activity between liposomes by microsomal triglyceride transfer protein, compds. of this invention showed IC50 values of < 10 nM to 1000 nM. Formulations are given.

IT 107133-36-8, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of biphenyl or phenylheterocyclyl moiety-containing esters (as inhibitors of microsomal triglyceride transfer protein) and α- and β-blockers)

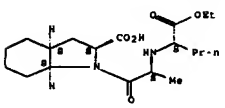
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 91 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:200816 CAPLUS Full-text

DN 142:430514

TI 2'-Benzothiazolylthioesters of N-substituted alpha amino acids: versatile intermediates for synthesis of ACE inhibitors

AU Singh, Girij Pal; Godbole, Himanshu M.; Nehate, Sagar P.; Mahajan, Pravin R.

CS Lupin Research Park, Lupin Ltd., Pune, India

SO Synthetic Communications (2005), 35(2), 243-248
CODEN: SYNCAV; ISSN: 0039-7911

PB Taylor & Francis, Inc.

DT Journal

LA English

OS CASREACT 142:430514

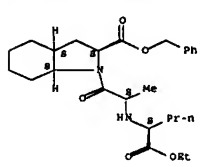
AB ACE (angiotensin-converting enzyme) inhibitors have been synthesized in high diastereomeric selectivity by condensation of novel activated amino esters with cyclic amino acid esters using simple reaction conditions. The activated amino esters may be obtained from the corresponding carboxylic acids or their acid chlorides by activation with 2-mercapto-benzothiazole.

IT 122454-52-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of ACE inhibitors by condensation of mercaptobenzothiazole-activated esters with cyclic amino esters)

RN 122454-52-9 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

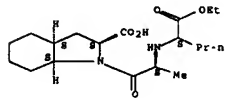


IT 82834-16-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of ACE inhibitors by condensation of mercaptobenzothiazole-activated esters with cyclic amino esters)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

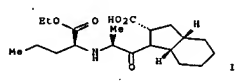


RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 92 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:182626 CAPLUS Full-text
DN 142:280052
TI Process for pure perindopril tert-butylamine salt
IN Parthasaradhi Reddy, Bandi; Rathnakar Reddy, Kura; Raji Reddy, Rapolu; Muralidhara Reddy, Dasari; Ramakrishna Reddy, Matta
PA Hetero Drugs Limited, India
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005019173	A1	20050303	WO 2003-IN276	20030821
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003263584	A1	20050310	AU 2003-263584	20030821
PRAI	WO 2003-IN276	A	20030821		

GI



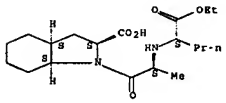
I

AB Pure perindopril tert-butylamine salt is obtained by extracting an aqueous solution of perindopril (I), namely (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid, or its salt contaminated with impurities with a suitable organic solvent such as methylene dichloride at a pH of 4.0 to 6.5, separating the organic layer, isolating I from the organic layer and converting it into tert-butylamine salt. Thus, perindopril tert-butylamine salt (15 g, purity 92.4%) was added to water (100 mL) and CH2Cl2 (100 mL) and the pH of the mass was adjusted to 5.4 by using 20% dilute HCl. The phases were separated and the aqueous layer was washed with CH2Cl2 (2 x 75 mL). The CH2Cl2 layer and washings are combined and the combined organic phase was washed with water (50 mL) and then with 10% aqueous NaCl (50 mL). The organic layer was dried over Na2SO4 and concentrated to give a residue, perindopril, (99.3 % purity). EtOAc (255 mL) was added to the residue (15 g) and stirred for 10 min to obtain a clear solution. tert-Butylamine was added dropwise to the solution at 30° and stirred for 1 h at the same temperature. The reaction mass was then

heated to reflux, passed over hiflo rapidly at reflux temperature and washed with hot EtOAc (30 mL). Then, the reaction mass was stirred for 2 h at .apprx.30°, cooled to 0°, and stirred for further 2 h at 0° to 5°. The separated solid was filtered, washed with EtOAc (15 mL), and dried to give 12 g of 99.77% pure perindopril tert-butylamine salt.

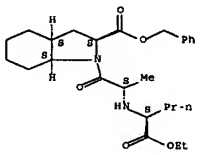
IT 82834-16-0P, Perindopril 122454-52-8P, (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(Ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylic acid benzyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; process for pure perindopril tert-butylamine salt)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

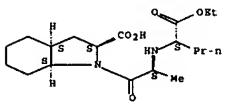


IT 107133-36-8P, Perindopril tert-butylamine salt
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for pure perindopril tert-butylamine salt)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

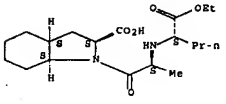
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 93 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:177840 CAPLUS Full-text
DN 142:274011
TI Nitrosated and nitrosylated cardiovascular compounds, their compositions, and use
IN Garvey, David S.; Letts, Gordon L.; Worcel, Manuel; Gaston, Ricky D.
PA Nitromed, Inc., USA
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005018561	A2	20050303	WO 2004-US26909	20040820
	WO 2005018561	A3	20050721		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004266705	A1	20050303	AU 2004-266705	20040820
	CA 2536173	A1	20050303	CA 2004-2536173	20040820
	EP 1670459	A2	20060621	EP 2004-781569	20040820
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	JP 2007502831	T	20070215	JP 2006-524034	20040820
	US 2007010571	A1	20070111	US 2006-569077	20060221
PRAI	US 2003-496639P	P	20030820		
	US 2003-496722P	P	20030820		
	US 2003-496810P	P	20030821		
	US 2003-498291P	P	20030828		
	US 2003-498308P	P	20030828		
	US 2003-530643P	P	20031219		
	WO 2004-US26909	W	20040820		

OS MARPAT 142:274011
AB Compns. and kits are described, comprising a nitrosated and/or nitrosylated cardiovascular compound, a nitric oxide donor compound and/or another therapeutic agent for treating cardiovascular diseases, renovascular diseases, diabetes, diseases resulting from oxidative stress, endothelial dysfunctions, diseases caused by endothelial dysfunctions, cirrhosis, pre-eclampsia, osteoporosis, and nephropathy. The nitrosated and/or nitrosylated cardiovascular compds. are preferably β-adrenergic antagonists, ACE inhibitors, anti-hyperlipidemic compds., or antithrombotic and vasodilator compds.
IT 82834-16-0D, Perindopril, nitrosated and nitrosylated derivs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitrosated and nitrosylated cardiovascular compds., their compns., and use)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

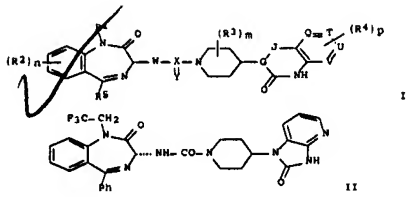


L8 ANSWER 94 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:136493 CAPLUS Full-text
DN 142:240471
TI Preparation of benzodiazepine derivatives as CGRP receptor antagonists
IN Burgey, Christopher S.; Stump, Craig A.; Williams, Theresa M.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005013894	A2	20050217	WO 2004-US20209	20040624
	WO 2005013894	A3	20060302		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004260630	A1	20050217	AU 2004-260630	20040624
	CA 2529196	A1	20050217	CA 2004-2529196	20040624
	EP 1641423	A2	20060405	EP 2004-776997	20040624
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1842526	A	20061004	CN 2004-80017996	20040624
	JP 2007516183	T	20070621	JP 2006-517599	20040624
	US 2006135511	A1	20060622	US 2005-562297	20051222
PRAI	US 2003-482654P	P	20030626		
	WO 2004-US20209	W	20040624		

OS CASREACT 142:240471; MARPAT 142:240471
GI



I

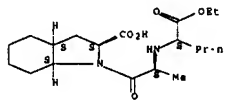
II

AB Benzodiazepine derivs. of formula I [R1 = H, alkyl, cycloalkyl, aryl, etc.; R2 = H, alkyl, cycloalkyl, aryl, etc.; R3 = H, alkyl, CO2H, alkoxycarbonyl; R4 = H, alkyl, cycloalkyl, aryl, etc.; R5 = H, alkyl, cycloalkyl, etc.; n = 1-4; m = 1-9; p = 1-4; W = O, (substituted) NH, (substituted) CH2; X = C, S; Y = O, NCONH2, etc.; G, J = N, NCH2, etc.; Q, T, U, V = CH, N; with provisos] are prepared as antagonists of CGRP receptors, and are useful in the treatment or prevention of diseases in which the CGRP is involved, such as headache, migraine and cluster headache. The invention is also directed to

pharmaceutical compns. comprising these compds. and the use of these compds. and compns. in the prevention or treatment of such diseases in which CGRP is involved. Thus, II was prepared in several steps. The prepared compds. had IC50 values < 50 μM against CGRP receptor.

IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agent for co-administration with benzodiazepines)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

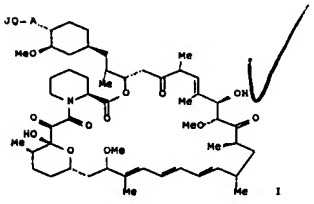


L4 ANSWER 95 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:122803 CAPLUS Full-text
DN 142:219083
TI Preparation of phosphorus-containing rapamycin derivatives for use in pharmaceutical compositions as immunosuppressive and anticancer agents
IN Metcalf, Chester A., III; Rozamus, Leonard W.; Wang, Yihan; Berstein, David L.
PA Ariad Gene Therapeutics, Inc., USA
SO U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of U.S. Ser. No. 635,054.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005032825	A1	20050210	US 2004-862149	20040604
	US 7091213	B2	20060815		
	US 2003220297	A1	20031127	US 2003-357152	20030203
	US 2004073024	A1	20040415	US 2003-635054	20030806
	US 2006264405	A1	20061123	US 2006-429582	20060505
	US 2006264456	A1	20061123	US 2006-494418	20060727
	US 7186826	B2	20070306		
	US 2007190106	A1	20070816	US 2007-650017	20070105
PRAI	US 2002-353252P	P	20020201		
	US 2002-426928P	P	20021115		
	US 2002-428383P	P	20021122		
	US 2002-433930P	P	20021217		
	US 2003-357152	A2	20030203		
	US 2003-635054	A2	20030806		
	US 2003-486367P	P	20030711		
	US 2004-862149	A2	20040604		
	US 2004-889163	B2	20040712		
	US 2005-711859P	P	20050826		

	US 2006-494418	A1	20060727		

OS CASREACT 142:219083; MARPAT 142:219083
GI

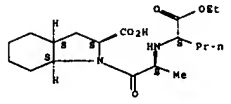


I

AB Rapamycin derivs. containing phosphorus moiety, such as I [A = O, S, NR2, absent; Q = V, OV, SV, NR2, absent; V = aliphatic, heteroaliph., aryl, heteroaryl moiety, such that J is linked to the cyclohexyl ring directly, through A or through VA, OVA, SVA or NR2VA; J = P(:K)(YR5)2, P(YR5)2, P(:K)(YR5)OR6; K = O, S; Y = O, S, NR2, bond; R2, R5 = aliphatic, heteroaliph., aryl, heteroaryl, H; R6 = PK(YR5)YR5, SO2YR5, C(O)YR5; G = O, S, NR2, (M)X; M = (un)substituted methylene, alkyl, alkylene; X = 1-6], and pharmaceutically acceptable derivs. thereof, were prepared for therapeutic use as immunosuppressive and anticancer agents. These rapamycin derivs. are useful for treatment of graft vs. host disease, lupus, rheumatoid arthritis, diabetes mellitus, myasthenia gravis, multiple sclerosis, psoriasis, dermatitis, eczema, seborrhea, inflammatory bowel disease, pulmonary inflammation, ocular uveitis; adult T-cell leukemia, lymphoma, fungal infections, hyperproliferative restenosis, graft vascular atherosclerosis, coronary artery disease, cerebrovascular diseases, arteriosclerosis, atherosclerosis, nonatheromatous arteriosclerosis, or vascular wall damage from cellular events leading toward immune mediated vascular damage, stroke or multi-infarct dementia. Thus, I [A-QJ = OP(O)(OBu)Me] was prepared by reacting rapamycin with methylphosphonic dichloride and n-butanol using 3,5-lutidine in CH2Cl2 under a nitrogen atmospheric. Binding affinity of the rapamycin phosphorus derivs. for human FKBP-12 protein was assayed, dosages for restenosis prevention were discussed.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of phosphorus-containing rapamycin derivs. for use in pharmaceutical compns. as immunosuppressive and anticancer agents)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

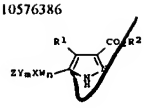


RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 96 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:120729 CAPLUS Full-text
DN 142:219276
TI Preparation of 5-substituted 2H-pyrazole-3-carboxylic acid derivatives as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases
IN Semple, Graeme; Gharbaoui, Tawfik; Shin, Young-Jun; Dascaire, Marc; Averbuj, Claudia; Skinner, Philip J.
PA Arena Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005011677	A1	20050210	WO 2004-US18389	20040610
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004260636	A1	20050210	AU 2004-260636	20040610
	CA 2528834	A1	20050210	CA 2004-2528834	20040610
	EP 1633351	A1	20060315	EP 2004-776418	20040610
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	US 2007032537	A1	20070208	US 2006-560332	20060908
PRAI	US 2003-478664P	P	20030613		
	WO 2004-US18389	W	20040610		

OS MARPAT 142:219276
GI



I

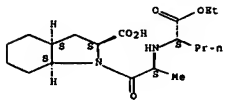
AB Title compds. [I; W, Y = (substituted) alkylene, alkenylene, alkynylene; X = NR3CO, NR3SO2, NR3, CO, CH(OH), C(NH), O, S, SO, SO2, etc.; R3, R4 = H, (substituted) alkyl, Ph, heteroaryl; Z = H, halo, (substituted) Ph, heteroaryl; R1 = H, OH, halo, alkyl, haloalkyl; R2 = H, alkyl; m, n = 0, 1; with provisos], were prepared Thus, 5-methylthiomethyl-2H-pyrazole-3-carboxylic acid (preparation outlined) showed hRUP25 agonist activity with EC50 = 4.3 μM.

IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of pyrazolecarboxylates as agonists for the RUP25 nicotinic acid receptor for the treatment of dyslipidemia and related diseases)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 97 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:99521 CAPLUS Full-text
DN 142:156329
TI Preparation of α-amino acid benzothiazolylthio esters as intermediates for manufacture of ACE inhibitors
IN Singh, Girij Pal; Godbole, Himanshu Madhav; Mahajan, Pravin Raghunath; Nehate, Sagar Purushottam
PA Lupin Limited, India
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005010028	A1	20050203	WO 2003-IN257	20030731

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

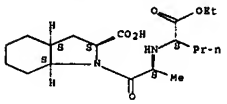
AU 2003272077 A1 20050214 AU 2003-272077 20030731
PRAI WO 2003-IN257 A 20030731
OS CASREACT 142:156329; MARPAT 142:156329
AB The invention relates to esters (S,S)-RCH2CH2CH(CO2R1)NHCHR2CO-X (I; R is alkyl or Ph; R1 H or alkyl; R2 is alkyl or aminoalkyl; X is 2-benzothiazolylthio) which are intermediates in the manufacture of ACE inhibitors I (X is an amino acid or derivative). The intermediate benzothiazolylthio esters were prepared by reaction of the appropriate acid or acid chloride with 2,2'-dithiobis(benzthiazole) or 2- mercaptobenzothiazole. Thus, treatment of N-[1(S)-(ethoxycarbonyl)-3- phenylpropyl]-N6-(trifluoroacetyl)-L-lysine (preparation given) with 2,2'-dithiobis(benzothiazole), followed by coupling with L-proline Et ester and deprotection, afforded lisinopril dihydrate.

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of α-amino acid benzothiazolylthio esters as intermediates for manufacture of ACE inhibitors)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



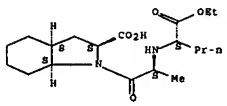
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

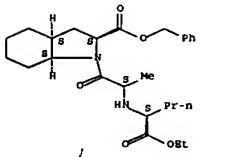
CRN 75-64-9
CMF C4 H11 N

IT 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of α-amino acid benzothiazolylthio esters as intermediates for manufacture of ACE inhibitors)

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 98 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:50771 CAPLUS Full-text
DN 142:107409

TI The use of inhibitors of the renin-angiotensin system for the prevention and treatment of stroke
IN Montgomery, Hugh Edward; Martin, John Francis; Erusalimsky, Jorge Daniel
PA Ark Therapeutics Limited, UK; Boehringer Ingelheim International GmbH
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1498124	A2	20050119	EP 2004-21889	19981019
EP 1498124	A3	20050817		
EP 1498124	B1	20070704		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
EP 1023067	A2	20000802	EP 1998-947698	19981019
EP 1023067	B1	20050504		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1123342	B	20031008	CN 1998-811314	19981019
EP 1559424	A2	20050803	EP 2005-9398	19981019
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
ES 2238770	T3	20050901	ES 1998-947698	19981019
EP 1776954	A2	20070425	EP 2007-102160	19981019
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, AL, BA, HR, MK, YU				
AT 366110	T	20070715	AT 2004-21889	19981019
PRAI GB 1997-22026	A	19971017		
GB 1998-10855	A	19980520		
EP 1998-947698	A3	19981019		
US 1997-67819P	P	19971205		
US 1998-94902P	P	19980731		
EP 2004-21889	A3	19981019		
WO 1998-GB3122	W	19981019		

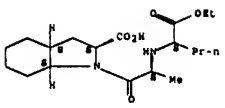
AB An inhibitor of the renin-angiotensin system is used for the manufacture of a medicament for the treatment or prevention of stroke or its recurrence. The inhibitor is selected from quinapril, captopril, lisinopril, perindopril, trandolapril, enalapril, moexipril, fosinopril, ramipril, cilazapril, imidapril, spirapril, temocapril, benazepril, alacepril, ceronapril, delapril, moveltipril, trandolapril, losartan, valsartan, irbesartan, candesartan, eprosartan, tasosartan and telmisartan.

IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(renin-angiotensin system inhibitors for prevention and treatment of stroke)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

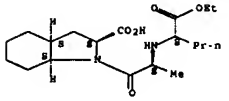
Absolute stereochemistry. Rotation (-).



L8 ANSWER 99 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:43552 CAPLUS Full-text
DN 142:259096
TI Effects of perindopril treatment on hemostatic function in patients with essential hypertension in relation to angiotensin converting enzyme (ACE) and plasminogen activator inhibitor-1 (PAI-1) gene polymorphisms
AU Jastrzebska, M.; Widecka, K.; Naruszewicz, M.; Ciechanowicz, A.; Janczak-Basan, A.; Poltynska, A.; Goracy, I.; Chetstowski, K.; Wesotowska, T.
CS Chair of Clinical Biochemistry, Pomeranian Medical University, Szczecin, Pol.
SO Nutrition, Metabolism and Cardiovascular Diseases (2004), 14(5), 259-269
CODEN: NMCDEE; ISSN: 0939-4753
PB Medikal Press
DT Journal
LA English
AB An imbalance in the hemostatic system is a frequent finding in untreated essential hypertension (HT), and it has been shown that treatment with angiotensin converting enzyme (ACE) inhibitors improves hemostatic function. In order to elucidate the role of genetic factors, we studied hemostasis in patients with untreated and treated HT and correlated the results with ACE I/D and plasminogen activator inhibitor-1 (PAI-1) 4G/5G gene polymorphisms. Forty-three males with HT (mean age 31.7±6.8 years)were compared with 34 age and gender-matched controls. All of the patients were treated with perindopril (4 mg/day) and, after one and six months of therapy, their levels of plasma fibrinogen (Fb), t-PA antigen, PAI-1 antigen, von Willebrand factor (vWF), ACE activity and blood pressure were measured. ACE and PAI-1 genotypes were identified by means of the polymerase chain reaction on DNA isolated from peripheral blood lymphocytes. Untreated patients had significantly higher levels of Fb, PAI-1 ($p<0.01$) and t-PA ($p<0.05$) regardless of their ACE or PAI-1 genotypes. Perindopril reduced blood pressure regardless of ACE or PAI-1 genotype ($p<0.001$). ACE II homozygotes showed the greatest decrease in ACE activity ($p<0.01$) and a significant reduction in Fb levels ($p<0.05$) after just one month of treatment. Anal. of the group as a whole revealed an increase in t-PA antigen levels after six months of treatment, regardless of ACE of PAI-1 genotype ($p<0.01$). Our results show that essential hypertension predisposes to the procoagulant state characterized by hyperfibrinogenemia and hypofibrinolysis. Perindopril reduced fibrinogen levels in ACE II homozygotes due to its more potent inhibitory action on the renin-angiotensin system in such patients. It improved fibrinolysis by increasing t-PA levels regardless of ACE and PAI-1 genotype.
IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(perindopril reduced fibrinogen levels by inhibiting renin-angiotensin system in ACE II homozygotic hypertensive patient, increased t-PA levels thus improved fibrinolysis in hypertensive patient regardless of

ACE or PAI-1 genotype)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



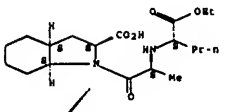
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 100 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:33235 CAPLUS Full-text
DN 142:128576
TI Detection of SNPs in human carboxyl esterase I gene for evaluation of drug metabolism
IN Ji, Gui-Jin; Muramatsu, Masaaki; Katagiri, Takashi; Shimotsukasa, Eiichi
PA Hubit Genomix Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 144 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2005006572	A	20050113	JP 2003-175498	20030619
PRAI JP 2003-175498		20030619		

AB This invention provides a process of detection of SNPs in human carboxyl esterase I gene. The DNA sequence for human carboxyl esterase I were disclosed. The SNPs occur at both promoter region and coding region of carboxyl esterase I gene. The method provided in this invention can be used for evaluation of angiotensin converting enzyme inhibitor metabolism in patients of hypertension, diabetic renal failure, cardiac insufficiency and juvenile pneumonia.
IT 82834-16-0, Perindopril
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor of, metabolism of; detection of SNPs in human carboxyl esterase I gene for evaluation of drug metabolism)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

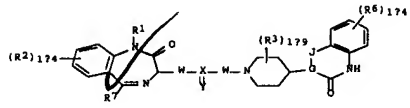
Absolute stereochemistry. Rotation (-).



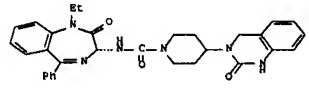
L8 ANSWER 101 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:14369 CAPLUS Full-text
DN 142:114110
TI Preparation of benzodiazepine CGRP receptor antagonists
IN Burgey, Christopher S.; Stump, Craig A.; Williams, Theresa M.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005000807	A2	20050106	WO 2004-US20206	20040624
WO 2005000807	A3	20060105		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004252150	A1	20050106	AU 2004-252150	20040624
CA 2529227	A1	20050106	CA 2004-2529227	20040624
EP 1641781	A2	20060405	EP 2004-776996	20040624
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1812982	A	20060802	CN 2004-80017952	20040624
JP 2007516182	T	20070621	JP 2006-517597	20040624
US 2006148790	A1	20060706	US 2005-562298	20051222
US 7196079	B2	20070327		
PRAI US 2003-482674P	P	20030626		
WO 2004-US20206	W	20040624		

OS CASREACT 142:114110; MARPAT 142:114110
GI



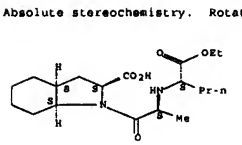
I



II

AB Title compds. I [R1 = H, alk(en/yn)yl, etc.; R2 = H, alkyl, cycloalkyl, etc.; R7 = H, alk(en/yn)yl, etc.; W = O, amino, alkyl; X = C, S; Y = O, NCN, etc.; R3 = H, alkyl, CN, etc.; R6 = H, alkyl, cycloalkyl, etc.; G-J = N, N-alkyl, etc.] are prepared For instance, II is prepared from (R)-3-amino-1-ethyl-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepine oxalate, p-nitrophenylchloroformate and 3-(piperidin-4-yl)-3,4- dihydroquinazolin-2(1H)-one hydrochloride. Compds. I exhibit affinity for the CGRP receptor with an IC50 of less than 50μM. I, alone or in combination with other agents, are useful for the treatment of diseases in which the CGRP is involved, such as headache, migraine and cluster headache.
IT 82834-16-0, Perindopril
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of benzodiazepine CGRP receptor antagonists for headaches)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 102 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1154670 CAPLUS Full-text
DN 142:62765

TI Preparation of various crystalline forms of perindopril erbumine for use as drug
IN Straessler, Christoph; Lenlek, Vit; Paessler, Roger
PA Azad Pharmaceutical Ingredients AG, Switz.
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004113293	A1	20041229	WO 2004-CH374	20040618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2530550	A1	20041208	CA 2004-2530550	20040618
AU 2004249345	A1	20041229	AU 2004-249345	20040618
EP 1636185	A1	20060322	EP 2004-737029	20040618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1812971	A	20060802	CN 2004-80017867	20040618
BR 2004011966	A	20060829	BR 2004-11966	20040618
JP 2007507418	T	20070329	JP 2006-515624	20040618
MX 2005PA13811	A	20060627	MX 2005-PA13811	20051216
NO 2006000256	A	20060118	NO 2006-256	20060118
US 2007135512	A1	20070614	US 2006-560464	20061128
PRAI CH 2003-1109	A	20030624		
WO 2004-CH374	W	20040618		

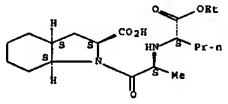
AB Disclosed are two novel crystalline forms d and e of perindopril erbumine, which are suitable as therapeutic substances in medicaments used for treating cardiovascular diseases, especially high blood pressure and cardiac insufficiency. Crystalline form e is obtained by crystallizing perindopril erbumine from MTBE containing 1.5 to 2.5 % (volume/volume) of water at 30 to 45°, preferably 34 to 45°, crystallization expediently taking place by stirring. Crystalline form e changes into crystalline form d if the water is removed, practically by azeotropic distillation, preferably at 35 to 37°, and stirring continues for at least 15 h at 30 to 45°, preferably 35 to 37°. Crystalline form d can also be obtained by stirring crystalline form a or ss in tert-Bu Me ether containing 0.9 to 1.4 % (volume/volume) of water at 33 to 38° while inoculating the same with crystalline form d. Crystalline form e can further be obtained by stirring crystalline form a or ss in tert-Bu Me ether containing 0.9 to 1.4 % (volume/volume) of water at 28 to 35° while inoculating the same with crystalline form e, or by stirring crystalline form a or ss in tert-Bu Me ether containing 1.5 to 2.0 % (volume/volume) of water at 35 to 38°.
IT 107133-36-8, Perindopril erbumine
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of various crystalline forms of perindopril erbumine for use as drug)
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 103 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1016010 CAPLUS Full-text
DN 141:424441
TI Process for the preparation of enalapril maleate and related compounds having ACE inhibitory action
IN Jenko, Branko
PA Lek Pharmaceuticals D.D., Slovenia
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

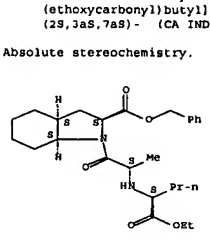
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004101515	A1	20041125	WO 2004-SI21	20040507
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

SI 21507	A	20041231	SI 2003-123	20030516
EP 1628956	A1	20060301	EP 2004-731808	20040507
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007072919	A1	20070329	US 2006-556986	20060929
PRAI SI 2003-123	A	20030516		
WO 2004-SI21	W	20040507		

OS MARPAT 141:424441
AB The invention relates to a process for the preparation of ACE-inhibitory peptides (S,S)-R1CH2CH2CH(CO2R2)-L-Ala-NR3R4 (R1 is H, alkyl, phenyl; R2 is H, alkyl; NR3R4 is a proline, 2-piperidinecarboxylic or hexahydro-2-azepinecarboxylic acid residue and related aza/thia analogs and their esters or metal salts) in which the carboxy group of (S,S)-R1CH2CH2CH(CO2R2)-L-Ala-OH is activated with a uronium salt in an aprotic solvent prior to coupling with an amino acid HNR3R4. Thus, a mixture of N-[1(S)-(ethoxycarbonyl)-3-phenylpropyl]-L-alanine, L-proline, Et3N and O-(benzotriazol-1-yl)-N,N,N'N'-tetramethyluronium hexafluorophosphate in acetonitrile-DMF was stirred for 30 min at room temperature to afford enalapril (85.4% yield of maleate).
IT 122454-52-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of enalapril maleate and related compds. having ACE inhibitory action)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

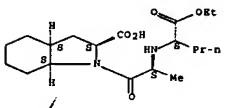
L8 ANSWER 104 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1009942 CAPLUS Full-text
DN 142:292431
TI Test kit, method and software for evaluating the pharmacodynamic effect of ACEI-like antihypertensive agent and its compounded medicine

IN Xing, Houxun; Jiang, Shanqun; Zhu, Guoying; Zhang, Minmin; Yu, Yunxian; Guang, Wenwei; Hong, Xiumei; Chen, Changzhong; Chen, Guangliang
PA Anhui Institute Of Biomedicine, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 23 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1472337	A	20040204	CN 2002-125863	20020731
CN 1679943	A	20051012	CN 2005-10008999	20020731
PRAI CN 2002-125863	A3	20020731		

AB The test kit consists of a pair of primers, endonuclease Hac III and its buffer II, PCR buffer, DNA polymerase Taq, and dNTPs. The PCR buffer is composed of KCl, Tris-HCl, and MgCl2. The buffer II is composed of Tris-HCl, MgCl2, NaCl, and DTT. The pharmacodynamic effect of ACEI-like antihypertensive agents is evaluated by using the test kit to analyze the genotype of polymorphous locus Asp919Gly of MS gene of homocysteine metabolic pathway. The software for evaluating the pharmacodynamic effect of ACEI-like antihypertensive agent is designed based on the genotype of MS gene, age, body mass, sex, height, basic diastolic pressure, basic systolic pressure, smoking history, etc. The compounded medicine for improving the pharmacodynamic effect of ACEI-like antihypertensive agent is composed of ACEI-like antihypertensive agent and synergist. The ACEI-like antihypertensive agent is captopril, enalapril, cilazapril, benazepril, perindopril, ramipril, fosinopril, and/or lisinopril. The synergist is folic acid, tetrahydrofolic acid, vitamin B12, vitamin B6, and/or their compounded preparation
IT 82834-16-0, Perindopril
RL: ANT (Analyte); ANST (Analytical study)
(test kit, method and software for evaluating pharmacodynamic effect of ACEI-like antihypertensive agent and its compounded medicine)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



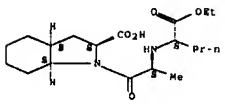
L8 ANSWER 105 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:996205 CAPLUS Full-text
DN 141:395815
TI A process for the preparation of perindopril using tetramethyluronium salts as coupling reagents
IN Rucman, Rudolf
PA Lek Pharmaceuticals D.D., Slovenia
SO PCT Int. Appl., 15 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004099236	A1	20041118	WO 2004-SI20	20040507
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21506	A	20041231	SI 2003-118	20030508
EP 1628995	A1	20060301	EP 2004-731809	20040507
EP 1628995	B1	20070627		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
AT 365745	T	20070715	AT 2004-731809	20040507
US 2007173637	A1	20070726	US 2006-555848	20061026
PRAI SI 2003-118	A	20030508		
WO 2004-SI20	W	20040507		

OS CASREACT 141:395815; MARPAT 141:395815
AB A process for the preparation of the ACE inhibitor perindopril involves activation of N-[1(S)-(ethoxycarbonyl)butyl]-(S)-alanine (1) with a tetramethyluronium salt in the presence of a tertiary organic base, coupling with (2S,3aS,7aS)-octahydroindole-2-carboxylic acid (2) or an ester, and deprotection. Thus, a mixture of 1, 2 benzyl ester, TBTU and diisopropylethylamine in DMF/CH2Cl2 was stirred for 4 h to afford benzyl-perindopril, which was converted to perindopril by phase transfer or classical hydrogenation.
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril using tetramethyluronium salts as coupling reagents)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

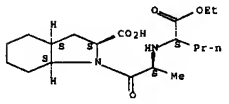


IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril using tetramethyluronium salts as coupling reagents)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

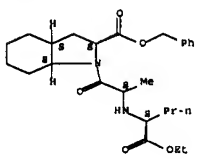


CM 2

CRN 75-64-9
CMF C4 H11 N

IT 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril using tetramethyluronium salts as coupling reagents)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

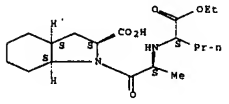
L8 ANSWER 106 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:996123 CAPLUS Full-text
DN 141:411226
TI Process for preparation of perindopril and its salts
IN Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra
PA Cipla Limited, India; Wain, Christopher Paul
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004099138	A2	20041118	WO 2004-GB2029	20040512
WO 2004099138	A3	20041223		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IN 2003MU00468	A	20050211	IN 2003-MU468	20030512
PRAI IN 2003-MU468	A	20030512		

OS CASREACT 141:411226; MARPAT 141:411226
AB A process for preparing perindopril or a pharmaceutically-acceptable salt comprises esterifying (2S,3aS,7aS)-octahydro-1H-indole-2-carboxylic acid (I) with benzyl alc. (or the 4-chloro or 4-alkoxy derivative) in the presence of benzenesulfonic acid as catalyst, treating the intermediate ester benzenesulfonate with N-[(S)-1-carbethoxybutyl]-L-alanine (II), and ester cleavage. Thus, I benzyl ester benzenesulfonate (40 g) was prepared, its suspension in CH2Cl2 made alkaline with aqueous ammonia, and the organic layer separated Treatment with II at 10-15 °C in the presence of hydroxybenzotriazole and N,N'-dicyclohexylcarbodiimide and workup afforded 43 g perindopril benzyl ester.
IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)
(preparation of perindopril and its salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

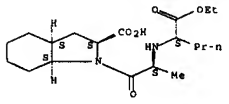


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



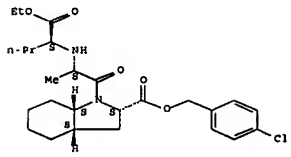
CM 2

CRN 75-64-9
CMF C4 H11 N

IT 793716-56-0 793716-57-1

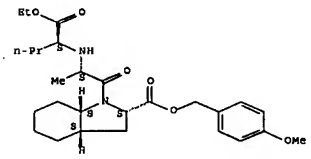
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of perindopril and its salts)
RN 793716-56-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (4-chlorophenyl)methyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



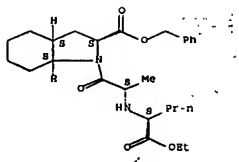
RN 793716-57-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (4-methoxyphenyl)methyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril and its salts)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



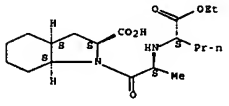
L8 ANSWER 107 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:908985 CAPLUS Full-text
DN 142:255716
TI Prediction of antihypertensive efficacy of angiotensin converting enzyme inhibitors based on the β2-adrenergic receptor (ADRB2) gene polymorphism
IN Xing, Houxun; Huang, Guo; Zhang, Yan; Peng, Shaojie; Li, Dong; Wang, Binyan; Chen, Guangliang; Huang, Aiqun; Wu, Di
PA Anhui Institute of Biomedicine, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1465712	A	20040107	CN 2002-123875	20020705
CN 1781554	A	20060607	CN 2005-10115552	20020705
PRAI CN 2002-123875	A3	20020705		

AB The test kit for evaluating the pharmacodynamic effect of angiotensin converting enzyme inhibitor (ACEI) type antihypertensives based on anal. of the polymorphism loci of β2-adrenergic receptor (ADRB2) gene consists of primer pair, endonuclease NcoI, endonuclease buffer 4, PCR buffer, thermostable DNA polymerase Taq, and dNTPs. The PCR buffer is composed of KCl, MgCl2, and tri(hydroxymethyl)aminomethane HCl (Tris-HCl). The endonuclease buffer 4 is composed of Tris-acetate, Mg(OAc)2, KOAc, and DTT. The method comprises extracting genomic DNA from host cell, PCR amplifying ADRB2 gene, digesting with endonuclease, detecting the genotype of Arg16Gly locus of ADRB2 gene by electrophoresis. The order of the blood pressure-lowering rate is homozygous mutation >heterozygous mutation >homozygous wild type. The method for designing the software for predicting the pharmacodynamic effect of ACEI type antihypertensives is presented. The medical composition is composed of ACEI type antihypertensive and β2-adrenergic receptor agonist or antagonist. The ACEI type antihypertensive is captopril, enalopril, cilazapril, benzazepril, perindopril, ramipril, fosinopril, lisinopril, losartan, and/or valsartan. The β2-adrenergic receptor agonist is salbutamol, terbutaline, procaterol, formoterol, clorprenaline, and/or salmeterol. The β2-adrenergic receptor antagonist is propranolol, labetalol, nadolol, and/or celiprolol.
IT 82834-16-0, Perindopril
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(prediction of antihypertensive efficacy of angiotensin converting enzyme inhibitors based on β2-adrenergic receptor (ADRB2) gene

polymorphism)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



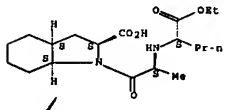
L8 ANSWER 108 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:799452 CAPLUS Full-text
DN 141:301435
TI Acidic drug complexes for improved bioavailability and delivery
IN Yu, Ruey J.; Van Scott, Eugene J.
PA USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004082628	A2	20040930	WO 2004-US8112	20040317
WO 2004082628	A3	20041119		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004220264	A1	20041104	US 2004-801134	20040316
AU 2004222305	A1	20040930	AU 2004-222305	20040317
CA 2519126	A1	20040930	CA 2004-2519126	20040317
EP 1603549	A2	20051214	EP 2004-757550	20040317
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
PRAI US 2003-454631P	P	20030317		
US 2004-801134	A	20040316		
WO 2004-US8112	A	20040317		

OS MARPAT 141:301435
AB Embodiments of the invention relate to a composition, a process of making the composition, and to the use of the composition. The compns. include a mol. complex formed between an acidic pharmaceutical drug and at least one

functional substance. The compns. provide improved bioavailability and improved delivery of the drug into the cutaneous tissues. For example, methotrexate complex with L-lysine was found to have less skin irritation when applying topically to treat psoriasis on the forearm.
IT 82834-16-0D, Perindopril, complexes with amino acid derivs.
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(topical compns. containing acidic active ingredient complexes with amino acids and their derivs. for improved skin care and treatment of skin conditions)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 109 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:740158 CAPLUS Full-text
DN 141:243833
TI Process for preparation of perindopril and its salts
IN Datta, Debashish; Singh, Girij Pal; Godbole, Himanshu Madhav; Siyan, Rajinder Singh
PA Lupin Limited, India
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004075889	A1	20040910	WO 2003-IN42	20030228
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2517205	A1	20040910	CA 2003-2517205	20030228
AU 2003224420	A1	20040917	AU 2003-224420	20030228
EP 1603558	A1	20051214	EP 2003-720846	20030228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

	JP 2006519168	T	20060824	JP 2004-568714	20030228
	US 2006276659	A1	20061207	US 2006-547243	20060621
PRAI	WO 2003-IN42	W	20030228		

OS CASREACT 141:243833; MARPAT 141:243833

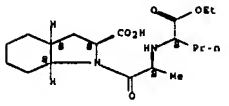
AB A process for the preparation of perindopril and its salts involves reaction of N-[1(S)-(ethoxycarbonyl)butyl]-L-alanyl chloride (I) or bromide with (2S)-indolinecarboxylic acid benzyl ester or its hexahydro derivative, followed by catalytic hydrogenation. Thus, perindopril benzyl ester was prepared by adding a slurry of 1.88 g I (preparation given) to a solution of 1.6 g (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester and triethylamine in CH2Cl2 at -10 to 15° over 25-30 min. Hydrogenation of the benzyl ester over 10% Pd-C afforded 1.3 g perindopril.

IT 82834-16-0, Perindopril
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril and its salts)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

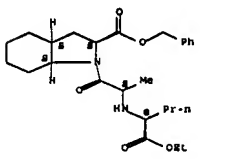


IT 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril and its salts)

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 110 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:676310 CAPLUS Full-text

DN 141:238870

TI Inhibition of angiotensin I-converting enzyme induces radioprotection by preserving murine hematopoietic short-term reconstituting cells

AU Charrier, Sabine; Michaud, Annie; Badaoui, Sabrina; Giroux, Sebastien; Ezan, Eric; Sainteny, Francoise; Corvol, Pierre; Vainchenker, William

CS Institut National de la Sante et de la Recherche Medicale (INSERM), Hematopoiese et Cellules Souches, Institut Gustave Roussy, Villejuif, Fr.

SO Blood (2004), 104(4), 978-985
CODEN: BLOOAN; ISSN: 0006-4971

PB American Society of Hematology

DT Journal

LA English

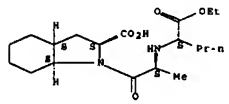
AB Angiotensin I-converting enzyme (ACE) inhibitors can affect hematopoiesis by several mechanisms including inhibition of angiotensin II formation and increasing plasma concns. of AcSDKP (acetyl-N-Ser-Asp-Lys-Pro), an ACE substrate and a neg. regulator of hematopoiesis. We tested whether ACE inhibition could decrease the hematopoietic toxicity of lethal or sublethal irradiation protocols. In all cases, short treatment with the ACE inhibitor perindopril protected against irradiation-induced death. ACE inhibition accelerated hematopoietic recovery and led to a significant increase in platelet and red cell counts. Pretreatment with perindopril increased bone marrow cellularity and the number of hematopoietic progenitors (granulocyte macrophage colony-forming unit [CFU-GM], erythroid burst-forming unit [BFU-E], and megakaryocyte colony-forming unit [CFU-MK]) from day 7 to 28 after irradiation. Perindopril also increased the number of hematopoietic stem cells with at least a short-term reconstitutive activity in animals that recovered from irradiation. To determine the mechanism of action involved, we evaluated the effects of increasing AcSDKP plasma concns. and of an angiotensin II type 1 (AT1) receptor antagonist (telmisartan) on radioprotection. We found that the AT1-receptor antagonism mediated similar radioprotection as the ACE inhibitor. These results suggest that ACE inhibitors and AT1-receptor antagonists could be used to decrease the hematopoietic toxicity of irradiation

IT 82834-16-0, Perindopril
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE inhibition induces radioprotection by preserving hematopoietic short-term reconstituting cells)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 111 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:490720 CAPLUS Full-text

DN 141:59698

TI ACE inhibitors having antioxidant and NO-donor activity and use for cardiovascular, renal and diabetes-associated disorders

IN Haj-Yehia, Abdullah Ibrahim; Khan, Mohamed Amin; Qadri, Bashir Ali

PA Yissum Research Development Company of the Hebrew University of Jerusalem, Israel

SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004050084	A2	20040617	WO 2003-IL1006	20031127
	WO 2004050084	A3	20040930		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003286389	A1	20040623	AU 2003-286389	20031127
	EP 1578413	A2	20050928	EP 2003-777134	20031127
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2006166894	A1	20060727	US 2005-536628	20051219
PRAI	US 2002-429864P	P	20021129		
	US 2002-430003P	P	20021129		
	WO 2003-IL1006	W	20031127		

OS MARPAT 141:59698

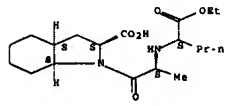
AB The present invention provides multifunctional ACE inhibitor compds. that combine ACE-inhibiting activity with capability to scavenge superoxide and other reactive oxygen species, and that may further function as nitric oxide (NO) donors. The compds. are useful for preventing or treating various disorders, including cardiovascular, and diabetes-associated disorders. This invention is further directed to a method for treating and preventing a disorder in which treatment with an ACE inhibitor is indicated, and mainly cardiovascular disorders, renal disorders, and diabetes-associated disorders. The use of said compds. in the preparation of a medicament is further provided.

IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE inhibitors having antioxidant and NO-donor activity and use for cardiovascular, renal and diabetes-associated disorders)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 112 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:427629 CAPLUS Full-text

DN 140:407114

TI Method for synthesis of perindopril and its pharmaceutically-acceptable salts

IN Dubuffet, Thierry; Langlois, Pascal

PA Lee Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1422236	A1	20040526	EP 2003-292865	20031119
	EP 1422236	B1	20070214		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 353910	T	20070315	AT 2003-292865	20031119
	ES 2282587	T3	20071016	ES 2003-3292865	20031119
	WO 2005054277	A1	20050616	WO 2004-FR2937	20041118
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	EP 2003-292865	A	20031119		

OS MARPAT 140:407114

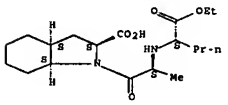
AB Perindopril was prepared by cyclization of (2S)-3-(2-bromophenyl)-2-[[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]propanoyl]amino]propanoic acid (I) or its esters in the presence of a Pd-based catalyst and a base (e.g., Pd2(dba)3, P(o-tolyl)3, and Cs2CO3], followed by catalytic hydrogenation. Intermediate I was prepared by coupling of N-[(S)-1-carbethoxybutyl]-L- alanine N-carboxyanhydride with (S)-2-bromophenylalanine.

IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

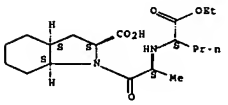


IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

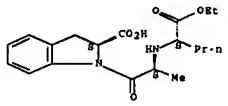


CM 2

CRN 75-64-9
CMF C4 H11 N

IT 685141-30-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 685141-30-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3-dihydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



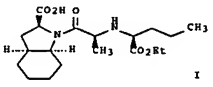
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 113 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:405692 CAPLUS Full-text
DN 140:407109
TI Hydrogenolysis of benzyl ester of perindopril for preparing perindopril monohydrates for use as inhibitors of angiotensin converting enzyme (ACE)
IN Rao, Dhanmaraj Ramachandra; Kankan, Rajendra Narayanrao
PA Cipla Limited, India
SO Brit. UK Pat. Appl., 16 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

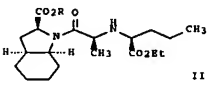
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2395195	A	20040519	GB 2002-26885	20021118
CA 2506587	A1	20040603	CA 2003-2506587	20031118
WO 2004046172	A1	20040603	WO 2003-GB4981	20031118
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003283588	A1	20040615	AU 2003-283588	20031118
EP 1565485	A1	20050824	EP 2003-775565	20031118
EP 1565485	B1	20070124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015703	A	20051025	BR 2003-15703	20031118
CN 1738830	A	20060222	CN 2003-80108700	20031118

EP 1688427	A1	20060809	EP 2006-76083	20031118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LV, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
JP 2006520320	T	20060907	JP 2004-552875	20031118
AT 352555	T	20070215	AT 2003-775565	20031118
CN 1966519	A	20070523	CN 2006-10168603	20031118
ES 2279188	T3	20070816	ES 2003-3775565	20031118
MX 2005PA05333	A	20050816	MX 2005-PA5333	20050518
IN 2005MN00599	A	20051007	IN 2005-MN599	20050613
US 2006063941	A1	20060323	US 2005-535187	20051031
IN 2006MN01471	A	20070824	IN 2006-MN1471	20061204
PRAI GB 2002-26885	A	20021118		
CN 2003-80108700	A3	20031118		
EP 2003-775565	A3	20031118		
WO 2003-GB4981	W	20031118		
IN 2005-MN599	A3	20050613		

OS CASREACT 140:407109; MARPAT 140:407109
GI



I



II

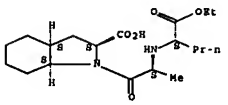
AB Perindopril (I), or a pharmaceutically acceptable salt thereof, may be prepared from a protected ester II (R = aralkyl, CH2Ph) via hydrogenolysis in the presence of a noble metal catalyst, such as Pd/charcoal, in the presence of a base. For example, when the base is tert-butylamine, it forms a pharmaceutically-acceptable addition salt with I, thus forming perindopril erbumine, I·tert-butylamine salt. A monohydrate of I, or a pharmaceutically acceptable salt thereof, is also claimed and may be prepared by hydrating I, or a pharmaceutically acceptable salt thereof, by way of addition of water or by drying in air. Perindopril erbumine monohydrate was prepared and studied by x-ray diffraction. Perindopril monohydrates may be used as angiotensin converting enzyme (ACE) inhibitors.

IT 690267-47-1P, Perindopril erbumine monohydrate
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal structure; preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)
RN 690267-97-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

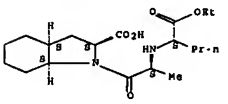


CM 2

CRN 75-64-9
CMF C4 H11 N

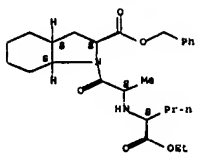
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 122454-52-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

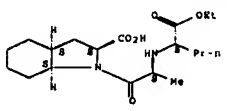


IT 107133-36-8P, Perindopril erbumine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril, its salts and monohydrates from hydrogenolysis of its benzyl ester)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

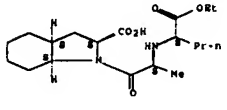
L8 ANSWER 114 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:405664 CAPLUS Full-text
DN 140:375492
TI Method for synthesis of (2S,3aS,7aS)-1-[(S)-alanyl]octahydro-1H-indole-2-carboxylic acid derivatives and use in the synthesis of perindopril
IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1420030	A2	20040519	EP 2003-293085	20031210
EP 1420030	A3	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004312186	A1	20050721	AU 2004-312186	20041209
CA 2548406	A1	20050721	CA 2004-2548406	20041209
WO 2005066199	A1	20050721	WO 2004-FR3167	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1890259	A	20070103	CN 2004-80036942	20041209
BR 2004017540	A	20070327	BR 2004-17540	20041209
IN 2006DN03063	A	20070824	IN 2006-DN3063	20060529
MX 2006PA06563	A	20060731	MX 2006-PA6563	20060609
US 2007123581	A1	20070531	US 2006-582419	20060609
US 7288661	B2	20071030		
NO 2006003027	A	20060628	NO 2006-3027	20060628
PRAI EP 2003-293085	A	20031210		
WO 2004-FR3167	W	20041209		

OS CASREACT 140:375492; MARPAT 140:375492
AB A method for the synthesis of the title perindopril intermediate involves coupling of (2S)-indoline-2-carboxylic acid benzyl ester or (2S,3aS,7aS)-octahydroindole-2-carboxylic acid benzyl ester or their salts with N-protected L-alanine in the presence of a coupling agent [e.g., O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate], followed by hydrogenation over Pd.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of alanyloctahydroindolecarboxylic acid derivs. in synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA

INDEX NAME)

Absolute stereochemistry. Rotation (-).



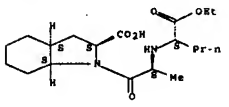
L8 ANSWER 115 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:405663 CAPLUS Full-text
DN 140:375491
TI Method for the synthesis of perindopril and its pharmaceutically-acceptable salts
IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1420029	A2	20040519	EP 2003-293084	20031210
EP 1420029	A3	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004312185	A1	20050721	AU 2004-312185	20041209
CA 2548405	A1	20050721	CA 2004-2548405	20041209
WO 2005066198	A1	20050721	WO 2004-FR3166	20041209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1890258	A	20070103	CN 2004-80036354	20041209
BR 2004017423	A	20070306	BR 2004-17423	20041209
IN 2006DN03069	A	20070824	IN 2006-DN3069	20060529
MX 2006PA06562	A	20060731	MX 2006-PA6562	20060609
US 2007093663	A1	20070426	US 2006-582283	20060609
US 7279583	B2	20071009		
NO 2006003012	A	20060628	NO 2006-3012	20060628
PRAI EP 2003-293084	A	20031210		
WO 2004-FR3166	W	20041209		

OS CASREACT 140:375491

AB A method for the synthesis of perindopril involves coupling of (2S)-indoline-2-carboxylic acid benzyl ester or (2S,3aS,7aS)- octahydroindole-2-carboxylic acid benzyl ester with N-[(S)-1- carbethoxybutyl]-L-alanine in the presence of a coupling agent [e.g., O-(benzotriazol-1-yl)-1,1,3,3-bis(tetramethylene)uronium hexafluorophosphate], followed by hydrogenation over Pd. Perindopril was converted into its tert-butylamine salt.
IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

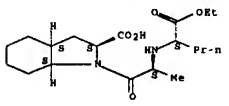


IT 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



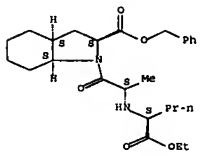
CM 2

CRN 75-64-9

CMF C4 H11 N

IT 122454-52-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

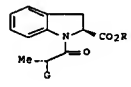


L8 ANSWER 116 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:405662 CAPLUS Full-text
DN 140:375490
TI Method for the synthesis of perindopril and its pharmaceutically-acceptable salts
IN Dubuffet, Thierry; Langlois, Pascal
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1420028	A2	20040519	EP 2003-292864	20031119
	EP 1420028	A3	20040526		
	EP 1420028	B1	20070221		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 354586	T	20070315	AT 2003-292864	20031119
	ES 2282586	T3	20071016	ES 2003-3292864	20031119
	AU 2004295132	A1	20050616	AU 2004-295132	20041118
	CA 2546506	A1	20050616	CA 2004-2546506	20041118

	WO 2005054276	A1	20050616	WO 2004-FR2936	20041118
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1882607	A	20061220	CN 2004-80033686	20041118
	BR 2004016746	A	20070116	BR 2004-16746	20041118
	IN 2006DN02563	A	20070810	IN 2006-DN2563	20060508
	MX 2006PA05607	A	20060817	MX 2006-PA5607	20060518
	US 2007083052	A1	20070412	US 2006-580148	20060518
	US 7208607	B1	20070424		
	NO 2006002599	A	20060606	NO 2006-2599	20060606
PRAI	EP 2003-292864	A	20031119		
	WO 2004-FR2936	W	20041118		

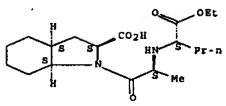
OS CASREACT 140:375490; MARPAT 140:375490
GI



I

AB A method for the synthesis of perindopril involves reaction of indolinecarboxylate derivs. I (R = H or a protective group, G = Cl, Br, OH, TsO, MeSO3 or CF3SO3) with (S)-PrCH(NH2)CO2Et (II), followed by catalytic hydrogenation. II was prepared by reaction of (S)-2-BrC6H4CH2CH(NH2)CO2R with (R)-MeCH(G)COCl and intamol. coupling, e.g., in the presence of Pd2(dba)3, P(o-tolyl)3, and Cs2CO3. Perindopril was converted into its tert-butylamine salt.
IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

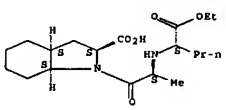


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

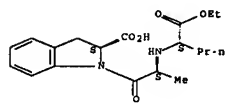


CM 2

CRN 75-64-9
CMF C4 H11 N

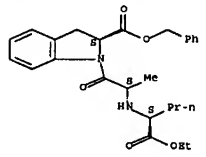
IT 685141-30-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 685141-30-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3-dihydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 685141-29-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 685141-29-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3-dihydro-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 117 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:333698 CAPLUS Full-text
DN 140:357333
TI Preparation of aroylhydroxypyrazoles for treatment of metabolic disorders
IN Semple, Graeme; Shin, Young Jun
PA Arena Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

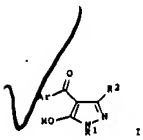
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004033431	A2	20040422	WO 2003-US31509	20031002
	WO 2004033431	A3	20040729		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2003282679	A1	20040504	AU 2003-282679	20031002
PRAI	US 2002-416193P	P	20021004		
	US 2002-417120P	P	20021007		
	WO 2003-US31509	W	20031002		

OS MARPAT 140:357333

GI



I

AB Title compds. [I; R1 = alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, benzyl, optionally substituted with ≥1 halo, OH, cyano, NO2, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl, alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfinyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalkylcylsulfonyl, alkylureyl, arylureyl; R2 = H, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, PhCH2, Ph, heteroaryl, optionally substituted with ≥1 halo, OH, cyano, nitro, haloalkyl, amino, aminoalkyl, aminodialkyl, alkyl, cycloalkyl, alkoxy, phenoxy, alkenyl, alkynyl, haloalkoxy, carboxy, carboalkoxy, alkylcarboxamido, arylcarboxamido, heteroarylcarboxamido, heterocyclic carboxamido, alkylthio, alkylsulfmyl, alkylsulfonyl, haloalkylthio, haloalkylsulfinyl, haloalkylsulfonyl, alkylureyl or arylureyl groups; Ar = (substituted) pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl], were prepared for the treatment of metabolic-related disorders, including dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance, type 2 diabetes, Syndrome-X and the like (no data). Thus, nicotinyl chloride, 2-methyl-5-propyl-2,4-dihydropyrazol-3-one, and Ca(OH)2 were heated at 90° in dioxane for 2 h, to give (5-hydroxy-1-methyl-3-propyl-1H- pyrazol-4-yl)pyridin-3-ylmethanone. I may be used in combination with other active agents such α-glucosidase inhibitors, aldose reductase inhibitors, biguanides, HMG-CoA reductase inhibitors, squalene synthesis inhibitors, fibrates, LDL catabolism enhancers, angiotensin converting enzyme inhibitors, and insulin secretion enhancers.

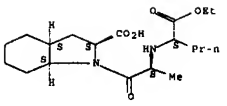
IT 2234-16-0, Perindopril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of aroylhydroxypyrazoles for treatment of metabolic disorders)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L16 ANSWER 118 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:266899 CAPLUS Full-text

DN 140:253919

TI Process for the synthesis of N-[(S)-1-(ethoxycarbonyl)butyl]-(S)-alanine for use in the synthesis of perindopril

IN Breard, Fabienne; Lecouve, Jean-Pierre

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1403278	A1	20040331	EP 2003-292404	20030930
	EP 1403278	B1	20050608		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 297407	T	20050615	AT 2003-292404	20030930
	PT 1403278	T	20050930	PT 2003-292404	20030930
	ES 2240926	T3	20051016	ES 2003-3292404	20030930
	WO 2005033127	A1	20050414	WO 2004-FR2463	20040929
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	EP 2003-292404	A	20030930		

OS MARPAT 140:253919

AB Perindopril intermediate (S)-EtO2CCHPr-L-Ala-OH was prepared by condensation of L-alanine alkyl or benzyl ester with Et glyoxylate or Et chloro(cyclohexyloxy)acetate, followed by allylation with allylzinc bromide, and catalytic hydrogenation.

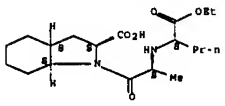
IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of [(ethoxycarbonyl)butyl]alanine for use in preparation of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 119 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:266898 CAPLUS Full-text

DN 140:253918

TI Method for synthesis of (2S,3aS,7aS)-1-[(S)-alanyl]octahydro-1H-indole-2-carboxylic acid derivatives for use in the synthesis of perindopril

IN Dubuffet, Thiery; Langlois, Pascal

PA Les Laboratoires Servier, Fr.; Servier Lab

SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1403277	A1	20040331	EP 2003-290486	20030228
	EP 1403277	B1	20051005		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 305939	T	20051015	AT 2003-290486	20030228
	PT 1403277	T	20051130	PT 2003-290486	20030228
	ES 2249691	T3	20060401	ES 2003-3290486	20030228
	AU 2004218202	A1	20040916	AU 2004-218202	20040227
	WO 2004078708	A2	20040916	WO 2004-FR445	20040227
	WO 2004078708	A3	20041014		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1753907	A	20060329	CN 2004-80005406	20040227
	JP 2006519176	T	20060824	JP 2006-500162	20040227
	IN 2005DN03205	A	20070525	IN 2005-DN3205	20050720
	US 2006149082	A1	20060706	US 2005-547132	20050824
	US 7157485	B2	20070102		
PRAI	EP 2003-290486	A	20030228		
	WO 2004-FR445	A	20040227		

OS CASREACT 140:253918; MARPAT 140:253918

AB A method for the synthesis of title perindopril intermediate involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indolecarboxylic acid (I) or an alkyl or

benzyl ester with N-protected alanine, followed by catalytic hydrogenation. I benzyl ester was prepared by reaction of 1-(1-cyclohexen-1-yl)pyrrolidine with (R)-ICH2CH(NBoc)CO2CH2Ph (Boc = tert-butoxycarbonyl), followed by deprotection and cyclization.

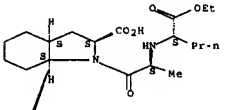
IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of alanyloctahydroindolecarboxylic acid derivs. for synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 120 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:266897 CAPLUS Full-text

DN 140:253917

TI Process for the synthesis of perindopril and its pharmaceutically-acceptable salts

IN Dubuffet, Thierry; Langlois, Pascal

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1403275	A1	20040331	EP 2003-290485	20030228
	EP 1403275	B1	20051019		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 307139	T	20051115	AT 2003-290485	20030228
	ES 2250846	T3	20060416	ES 2003-3290485	20030228
	AU 2004217599	A1	20040916	AU 2004-217599	20040227
	WO 2004078107	A2	20040916	WO 2004-FR446	20040227
	WO 2004078107	A3	20041021		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,				

GQ, GW, ML, MR, NE, SN, TD, TG

	CN 1753906	A	20060329	CN 2004-80005405	20040227
	JP 2006519177	T	20060824	JP 2006-500163	20040227
	IN 2005DN03206	A	20070525	IN 2005-DN3206	20050720
	US 2006149081	A1	20060706	US 2005-547131	20050824
	US 7166633	B2	20070123		
	HK 1086281	A1	20071005	HK 2006-106195	20060529
PRAI	EP 2003-290485	A	20030228		
	WO 2004-FR446	A	20040227		

OS MARPAT 140:253917

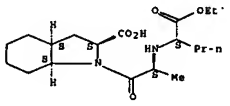
AB A method for the synthesis of perindopril involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H-indolecarboxylic acid (I) or an ester with N-[(S)-1-carbethoxybutyl]-L-alanine, followed by catalytic hydrogenation. I benzyl ester tosylate was prepared by reaction of 1-(1-cyclohexen-1- yl)pyrrolidine with (R)-ICH2CH(NBoc)CO2CH2Ph (Boc = tert-butoxycarbonyl), followed by deprotection and cyclization. Perindopril was converted into its tert-butylamine salt.

IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril and pharmaceutically-acceptable salts)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



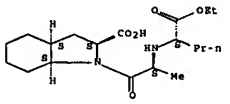
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

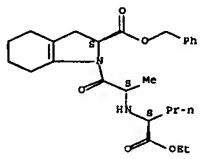
CRN 75-64-9
CMF C4 H11 N

IT 539820-43-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril and pharmaceutically-acceptable salts)

RN 539820-43-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 121 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:247009 CAPLUS Full-text
DN 140:253916
TI Process for the synthesis of N-[(S)-1-(ethoxycarbonyl)butyl]-(S)-alanine for use in preparation of perindopril
IN Breard, Fabienne; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	EP 1400531	A1	20040324	EP 2003-292405	20030930
	EP 1400531	B1	20060104		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 315046	T	20060215	AT 2003-292405	20030930
	ES 2256693	T3	20060716	ES 2003-292405	20030930
	WO 2005033128	A1	20050414	WO 2004-FR2464	20040929
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	EP 2003-292405	A	20030930		

OS MARPAT 140:253916

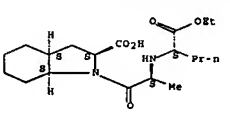
AB (S)-EtO2CCHPr-L-Ala-OH was prepared by a multistep procedure starting with allylation of Et glyoxylate with allylzinc bromide. Subsequent steps were resolution using Pseudomonas Fluorescens lipase, triflation of (R)-EtO2CCH(OH)CH2CH:CH2, substitution reaction with benzyl L-alaninate, and catalytic hydrogenolysis.

IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(process for synthesis of (carbethoxybutyl)-L-alanine in preparation of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

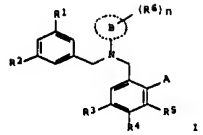
L6 ANSWER 122 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:203796 CAPLUS Full-text
DN 140:253571
TI Preparation of N-phenyl or N-heterocyclidibenzylamine compounds as inhibitors of cholesteryl ester transfer protein (CETP) and medicinal use thereof
IN Maeda, Kimiya; Nagamori, Hironobu; Nakamura, Hiroshi; Shinkai, Hisashi; Suzuki, Yasunori; Takahashi, Daisuke; Taniguchi, Toshio

PA Japan Tobacco Inc., Japan
SO PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004020393	A1	20040311	WO 2003-JP11041	20030829
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2464846	A1	20040311	CA 2003-2464846	20030829
	AU 2003261826	A1	20040319	AU 2003-261826	20030829
	BR 2003006208	A	20041013	BR 2003-6208	20030829
	JP 2004323504	A	20041118	JP 2003-308156	20030829
	JP 3630676	B2	20050316		
	CN 1617850	A	20050518	CN 2003-802383	20030829
	EP 1533292	A1	20050525	EP 2003-791414	20030829
	EP 1533292	B1	20070214		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	TR 200401413	T1	20050621	TR 2004-1413	20030829
	NZ 532494	A	20060331	NZ 2003-532494	20030829
	RU 2293078	C2	20070210	RU 2004-119546	20030829
	AT 353870	T	20070315	AT 2003-791414	20030829
	ES 2277142	T3	20070701	ES 2003-3791414	20030829
	EP 1829858	A2	20070905	EP 2007-3011	20030829
	EP 1829858	A3	20071003		
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR, AL, LT, LV, MK				
	ZA 2004003137	A	20050425	ZA 2004-3137	20040423
	IN 2004CN00889	A	20060113	IN 2004-CN889	20040428
	MX 2004PA05350	A	20040927	MX 2004-PA5350	20040603
	NO 2004002584	A	20040618	NO 2004-2584	20040618
	US 2005059810	A1	20050317	US 2004-503185	20041012
	HK 1077567	A1	20070914	HK 2005-109494	20051026
PRAI	JP 2002-255604	A	20020830		
	JP 2003-107161	A	20030410		
	EP 2003-791414	A3	20030829		
	WO 2003-JP11041	W	20030829		

OS MARPAT 140:253571

GI



I

AB Dibenzylamine compds. represented by the general formula (I) [R1, R2 = halo, NO2, cyano, C1-6 alkyl, halo-C1-6 alkyl; R3, R4, R5 = H, halo, each optionally halo-substituted C1-6 alkyl, C1-6 alkylthio, or C1-6 alkoxy; or R3 and R4 or R4 and R5 together with the carbon atoms bonded thereto form an (un)substituted halo- or heterocyclic ring; A = NR7R8; wherein R7, R8 = H, each (un)substituted C1-6 alkyl or C4-10 cycloalkyl, etc.; the ring B = aryl or heterocyclyl; R6 = H, halo, NO2, NH2, HO, cyano, acyl, C1-6 alkoxy, (un)substituted C2-6 alkenyl; n = an integer of 1-3] or prodrugs thereof or pharmaceutically acceptable salts thereof are prepared These compds. have selective and potent CETP inhibitory activity, which results in lowering intermediate-d. lipoprotein (IDL), very low d. lipoprotein (VLDL), and low d. lipoprotein (LDL) which promote arteriosclerosis, and increasing high d. lipoprotein (HDL), and are hence usable as, e.g., therapeutic or preventive drugs for hyperlipemia and arteriosclerosis. Thus, 17 mg NaH was added to a solution of 132 mg N-[3-(N-cyclopentylmethyl-N- ethylamino)-5,6,7,8-tetrahydronaphthalen-2-ylmethyl]-(2-methyl-2H-tetrazol- 5-yl)amine in 2 mL DMF, followed by adding 114 mg 3-bromomethyl-5- trifluoromethylbenzonitrile, and the resulting mixture was stirred at room temperature overnight to give, after workup and silica gel chromatog., 44% 3-[[N-[3-(N-cyclopentylmethyl-N-ethylamino)-5,6,7,8-tetrahydronaphthalen-2- ylmethyl]-N-(2-methyl-2H-tetrazol-5-yl)amino]methyl]-5- trifluoromethylbenzonitrile (II). II in vitro inhibited the activity of CETP in whole blood plasma with IC50 of 0.08 μM.

IT 107133-36-8, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antihypertensivs, combination therapy; preparation of N-Ph or N-heterocycclydibenzylamine compds. as inhibitors of cholesteryl ester transfer protein (CETP) for treatmsnt or prevention of hyperlipemia and arteriosclerosis)

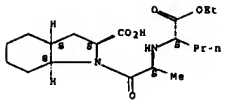
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absoluts stersochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 123 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:145230 CAPLUS Full-text
DN 141:218619
TI Rationale and design of a large-scale trial using nicorandil as an adjunct to percutaneous coronary intervention for ST-segment elevation acute myocardial infarction: Japan-working groups of acute myocardial infarction for the reduction of necrotic damags by a K-ATP channel opener (J-WIND-KATP)
AU Minamino, Tetsuo; Kim, Jiyoong; Asakura, Masanori; Shintani, Yasunori; Asanuma, Hiroshi; Kitakaze, Masafumi
CS J-WIND Investigators, Japan Foundation for Aging and Health for Medical Frontier Strategy Research by Health and Labor Sciences Research Grants, National Cardiovascular Center, Suits, Japan
SO Circulation Journal (2004), 68(2), 101-106
CODEN: CJIOBY; ISSN: 1346-9843
PB Japanese Circulation Society
DT Journal
LA English
AB Background: The benefits of percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI) are limited by reperfusion injury. In animal models, nicorandil, a hybrid of an ATP-sensitive K+ (KATP) channel opener and nitrates, reduces infarct size, so the Japan-Working groups of acute myocardial Infarction for the reduction of Necrotic Damage by a K-ATP channel opener (J-WIND-KATP) designed a prospective, randomized, multicenter study to evaluate whether nicorandil reduces myocardial infarct size and improves regional wall motion when used as an adjunctive therapy for AMI. Methods and Results: Twenty-six hospitals in Japan are participating in the J-WIND-KATP study. Patients with AMI who are candidates for PCI are randomly allocated to receive either i.v. nicorandil or placebo. The primary end-points are (1) estimated infarct size and (2) left ventricular function. Single nucleotide

polymorphisms (SNPs) that may be associated with the function of KATP-channel and the susceptibility of AMI to the drug will be examined Furthermore, a data mining method will be used to design the optimal combined therapy for post-myocardial infarction (MI) patients. Conclusions: It is intended that J-WIND-KATP will provide important data on the effects of nicorandil as an adjunct to PCI for AMI and that the SNPs information that will open ths field of tailor-made therapy. The optimal therapeutic drug combination will also be determined for post-MI patients.

IT 107133-36-8, Perindopril erbumine
RL: PAC (Pharmacological activity); THU (Therapsutic use); BIOL (Biological study); USES (Uses)
(nicorandil and cardiovascular agent for decreasing risk of cardiac events in patients with post-myocardial infarction)

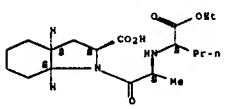
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 124 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:145229 CAPLUS Full-text
DN 141:219275
TI Rationale and design of a large-scale trial using atrial natriuretic peptide (ANP) as an adjunct to percutaneous coronary intervention for

ST-segment elevation acute myocardial infarction: Japan-working groups of acute myocardial infarction for the reduction of necrotic damage by ANP (J-WIND-ANP)
AU Asakura, Masanori; Kim, Jiyoong; Minamino, Tetsuo; Shintani, Yasunori; Asanuma, Hiroshi; Kitakaze, Masafumi
CS J-WIND Investigators, Japan Society for the Promotion of Sciencs for Young Scientists, Osaka University Graduate School of Medicine, Suita, Japan
SO Circulation Journal (2004), 68(2), 95-100
CODEN: CJIOBY; ISSN: 1346-9843
PB Japanese Circulation Society
DT Journal
LA English
AB Background: The benefits of percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI) are limited by reperfusion injury. In animal models, atrial natriuretic peptids (ANP) reduces infarct size, so the Japan-Working groups of acute myocardial Infarction for the reduction of Necrotic Damage by ANP (J-WIND-ANP) designed a prospective, randomized, multicenter study, to evaluate whether ANP as an adjunctive therapy for AMI reduces myocardial infarct size and improves regional wall motion. Methods and Results: Twenty hospitals in Japan will participate in the J-WIND-ANP study. Patients with AMI who are candidates for PCI are randomly allocated to receive either i.v. ANP or placebo administration. The primary end-points are (1) estimated infarct size (Σ-creatine kinase and troponin T) and (2) left ventricular function (left ventriculograms). Single nucleotide polymorphisms (SNPs) that may be associated with the function of ANP and susceptibility of AMI will be examined Furthermore, a data mining method will be used to design the optimal combinational therapy for post-MI patients. Conclusions: J-WIND-ANP will provide important data on the effects of ANP as an adjunct to PCI for AMI and the SNPs information will open the fisld of tailor-made therapy. The optimal therapeutic drug combination will also be determined for post-MI patients.

IT 107133-36-8, Perindopril erbumine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug therapy for data mining of cardiovascular therapy combination; large-scale trial rationale and design using atrial natriuretic peptide (ANP) as adjunct to PCI for ST-segment elevation acute myocardial infarction patients)

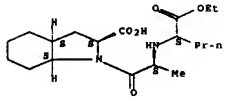
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

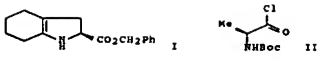
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 125 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:36709 CAPLUS Full-text
DN 140:59939
TI Method for synthesis of perindopril and its pharmaceutically acceptable salts
IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.; Servier Lab
SO Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1380591	A1	20040114	EP 2003-292132	20030829
	EP 1380591	B1	20051116		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 310012	T	20051215	AT 2003-292132	20030829
	ES 2252633	T3	20060516	ES 2003-3292132	20030829
	AU 2004270428	A1	20050317	AU 2004-270428	20040827
	WO 2005023842	A1	20050317	WO 2004-FR2197	20040827
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1835966	A	20060920	CN 2004-80023535	20040827
	JP 2007526902	T	20070920	JP 2006-524395	20040827
	IN 2006DN00922	A	20070810	IN 2006-DN922	20060222
	US 2007010572	A1	20070111	US 2006-569537	20060223
PRAI	EP 2003-292132	A	20030829		
	WO 2004-FR2197	W	20040827		

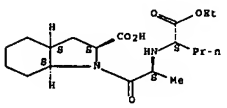
OS CASREACT 140:59939; MARPAT 140:59939

GI



AB A method for the synthesis of perindopril and its tert-Bu amine salt is described. The steps are: coupling of hexahydroindolecarboxylate I with propionyl chloride II in CH2Cl2, followed by Boc deprotection with TFA and reaction with Et 2-oxopentanoate and hydrogenation over Pd/C. Addition of tert-butylamine to perindopril provides the salt.
IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of perindopril and tert-butylamine salt)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

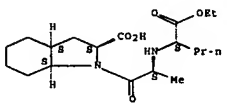


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 126 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:36708 CAPLUS Full-text
DN 140:59938
TI Method for synthesis of perindopril and its pharmaceutically acceptable salts
IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1380590	A1	20040114	EP 2003-292131	20030829
	EP 1380590	B1	20060906		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 338766	T	20060915	AT 2003-292131	20030829
	ES 2272922	T3	20070501	ES 2003-3292131	20030829
	AU 2004270427	A1	20050317	AU 2004-270427	20040827
	WO 2005023841	A1	20050317	WO 2004-FR2196	20040827
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				

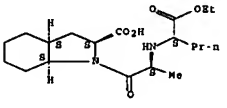
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	CN 1839147	A	20060927	CN 2004-80024192	20040827
	JP 2007526901	T	20070920	JP 2006-524394	20040827
	IN 2006DN00918	A	20070810	IN 2006-DN918	20060222
	US 2007043103	A1	20070222	US 2006-570566	20060227
	US 7183308	B1	20070227		
PRAI	EP 2003-292131	A	20030829		
	WO 2004-FR2196	W	20040827		

OS CASREACT 140:59938; MARPAT 140:59938

AB A method for the synthesis of perindopril and its pharmaceutically- acceptable salts involves coupling of (2S)-2,3,4,5,6,7-hexahydro-1H- indolecarboxylic acid or its benzyl ester with R2-L-Ala-X (R2 is a protective group, X is halo), followed by deprotection, reaction with (R)-PrCH(G)CO2Et (G is Cl, Br, I, or tosyloxy), and catalytic hydrogenation. Addition of tert-butylamine to perindopril provides the salt.
IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of perindopril and tert-butylamine salt)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

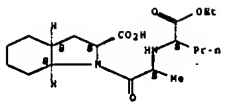


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).

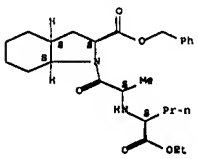


CM 2

CRN 75-64-9
CMF C4 H11 N

IT [illegible]
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril and tert-butylamine salt)
RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



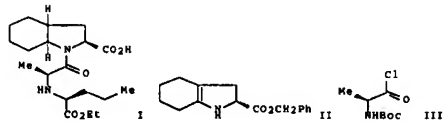
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 127 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:985781 CAPLUS Full-text
DN 140:28049
TI Method for synthesis of perindopril and its pharmaceutically acceptable

salts [2003/26]
IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.; Servier Lab
SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1371659	A1	20031217	EP 2003-292133	20030829
EP 1371659	B1	20051012		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 306496	T	20051015	AT 2003-292133	20030829
ES 2250853	T3	20060416	ES 2003-3292133	20030829
AU 2004270429	A1	20050317	AU 2004-270429	20040827
AU 2004270429	B2	20070524		
WO 2005023843	A1	20050317	WO 2004-FR2198	20040827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1835965	A	20060920	CN 2004-80023532	20040827
IN 2006DN00919	A	20070810	IN 2006-DN919	20060222
US 2007088168	A1	20070419	US 2006-570565	20060227
US 7223872	B2	20070529		
PRAI EP 2003-292133	A	20030829		
WO 2004-FR2198	W	20040827		

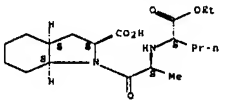
OS CASREACT 140:28049; MARPAT 140:28049
GI



AB A method for the synthesis of perindopril (I) and its tert-Bu amine salt is described. The steps are: coupling of (hexahydro)indolecarboxylate II with propionyl chloride III in CH2Cl2, followed by Boc deprotection with TFA, reaction with Et 2-oxopentanoate under reductive conditions, and removal of benzyl ester by hydrogenation to give I. Addition of tert-Bu amine to I provides the salt.

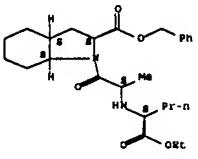
IT 82834-16-0P 122454-52-8P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of perindopril and its tert-Bu amine salt)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 122454-52-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

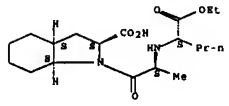


IT 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of perindopril and its tert-Bu amine salt)
RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 128 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:947713 CAPLUS Full-text
DN 139:381760
TI Method for synthesis of perindopril and its pharmaceutically acceptable salts
IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1367061	A1	20031203	EP 2003-291601	20030630
EP 1367061	B1	20060104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 315043	T	20060215	AT 2003-291601	20030630
ES 2256689	T3	20060716	ES 2003-3291601	20030630
AU 2004253721	A1	20050113	AU 2004-253721	20040628
WO 2005003153	A1	20050113	WO 2004-FR1637	20040628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	CN 1802384	A	20060712	CN 2004-80016014	20040628
	IN 2005DN05718	A	20070427	IN 2005-DN5718	20051209
	US 2006178421	A1	20060810	US 2005-562490	20051222
	US 7179833	B2	20070220		
PRAI	EP 2003-291601	A	20030630		
	WO 2004-FR1637	W	20040628		

OS CASREACT 139:381760; MARPAT 139:381760

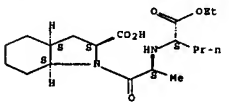
AB A method for the synthesis of perindopril and its pharmaceutically- acceptable salts (e.g., the tert-butylamine) involves cyclocondensation reaction of N-[(S)-1-carbethoxybutyl]-(S)-alanine with sulfinyl chlorides R1SOCl (R1 = imidazolyl, benimidazolyl, or tetrazolyl) to give Et (2S)-2-[(4S)-4-methyl-2,5-dioxo-1,2,3-oxathiazolidin-3-yl]pentanoate, which is amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid and hydrogenated over 10% Pt/C to give perindopril.

IT 82834-16-0P, Perindopril 107133-36-8P 122454-52-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of perindopril via cyclocondensation of carbethoxybutylalanine with imidazolesulfinyl chloride)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



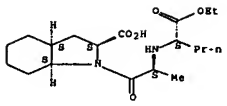
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



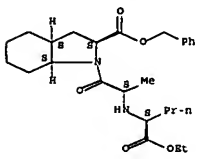
CM 2

CRN 75-64-9
CMF C4 H11 N

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.

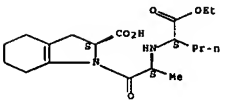


IT 625095-50-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of perindopril via cyclocondensation of carbethoxybutylalanine with imidazolesulfinyl chloride)

RN 625095-50-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 129 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:910218 CAPLUS Full-text

DN 139:365227

TI New process for the synthesis of N-[(S)-1-carboxybutyl]-(S)-alanine esters and their use in the synthesis of perindopril

IN Breard, Fabienne; Fugier, Claude

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1362845	A2	20031119	EP 2003-292145	20030901
	EP 1362845	A3	20040331		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AU 2004270432	A1	20050317	AU 2004-270432	20040831
	CA 2536926	A1	20050317	CA 2004-2536926	20040831
	WO 2005023755	A1	20050317	WO 2004-FR2213	20040831
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CN 1835911	A	20060920	CN 2004-80023534	20040831
	BR 2004013901	A	20061024	BR 2004-13901	20040831
	JP 2007504203	T	20070301	JP 2006-525159	20040831
	US 2006252958	A1	20061109	US 2006-569472	20060222
	MX 2006PA02229	A	20060517	MX 2006-PA2229	20060227
	NO 2006001152	A	20060310	NO 2006-1152	20060310
PRAI	EP 2003-292145	A	20030901		
	WO 2004-FR2213	W	20040831		

OS CASREACT 139:365227; MARPAT 139:365227

AB Title alanine derivs. (S)-RO2CCHPr-L-Ala-OH (R = C1-C6 alkyl) were prepared from N-protected (S)-5-methyl-2-morpholinone by propylation or allylation/hydrogenation, ring opening by LiOH, esterification, oxidation of

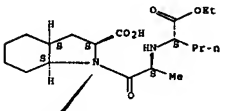
the hydroxy group, and deprotection. In an example, N-[(S)-1-carbethoxybutyl]-(S)-alanine hydrochloride was prepared via allylation of Boc-protected (S)-5-methyl-2-morpholinone and treatment of tert-Bu (3S,5S)-5-methyl-3-propyl-2-oxo-4-morpholinecarboxylate with LiOH in aqueous MeCN and then EtI to afford intermediate Et (2S)-2-[(tert- butoxycarbonyl)[(1S)-2-hydroxy-1-methylethyl]amino]pentanoate.

IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(process for synthesis of N-[(S)-carboxybutyl]-L-alanine esters for use in synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 130 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:909172 CAPLUS Full-text

DN 139:396166

TI Method for synthesis of perindopril and its pharmaceutically acceptable salts

IN Dubuffet, Thierry; Lecouve, Jean-Pierre

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1362864	A1	20031119	EP 2003-291600	20030630
	EP 1362864	B1	20070425		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 360638	T	20070515	AT 2003-291600	20030630
	AU 2004255899	A1	20050120	AU 2004-255899	20040628
	WO 2005005461	A2	20050120	WO 2004-FR1638	20040628
	WO 2005005461	A3	20050331		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,				

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CN 1805972	A	20060719	CN 2004-80016324		20040628
IN 2005DN05717	A	20070427	IN 2005-DN5717		20051209
US 2006148884	A1	20060706	US 2005-562950		20051223
US 7220776	B2	20070522			
PRAI EP 2003-291600	A	20030630			
WO 2004-FR1628	W	20040628			

OS CASREACT 139:396166; MARPAT 139:396166

AB Perindopril and its pharmaceutically acceptable salts (e.g., tert-butylamine salt) are prepared by the cyclocondensation reaction of N-[(S)-carboethoxy-1-butyl]-(S)-alanine with a carbonyl compound X1COX2 (X1, X2 = leaving group; e.g., 1,1'-carbonyldiimidazole) to give Et (2S)-2-[(4S)-4-Methyl-2,5-dioxo-1,3-oxazolidin-3-yl]pentanoate which is amidated with (2S)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylic acid in the presence of an acid (e.g., hydrochloric acid) to give (2S)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]-2,3,4,5,6,7- hexahydro-1H-indole-2-carboxylic acid which is hydrogenated with a 10% Pt/C catalyst to give perindopril which is then salified with tert-butylamine to give perindopril tert-butylammonium salt.

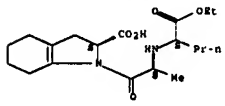
IT 625095-50-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; in a method for synthesis of perindopril and its pharmaceutically acceptable salts)

RN 625095-50-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, (2S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



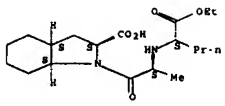
IT [illegible] Perindopril

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for synthesis of perindopril and its pharmaceutically acceptable salts)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 107133-36-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(method for synthesis of perindopril and its pharmaceutically acceptable salts)

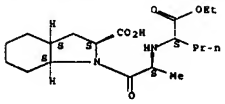
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 131 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:875244 CAPLUS Full-text
DN 139:364424

TI Method of preparing amine stereoisomers via reduction of sulfinylimines in presence of chiral auxiliaries

IN Han, Zhengxu; Krishnamurthy, Dhilsepkumar; Senanayake, Chris Hugh; Lu, Zhi-hui

PA Apsinterm, Llc., USA

SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2

DT Patent

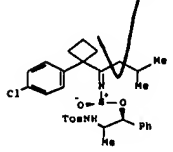
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003091207	A2	20031106	WO 2003-US8827	20030407
WO 2003091207	A3	20040916		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2482432	A1	20031106	CA 2003-2482432	20030407
AU 2003253588	A1	20031110	AU 2003-253588	20030407
EP 1497272	A2	20050119	EP 2003-747253	20030407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005522525	T	20050728	JP 2003-587772	20030407
CN 1659154	A	20050824	CN 2003-813204	20030407
IN 2004DN02806	A	20050401	IN 2004-DN2806	20040921
MX 2004PA09843	A	20050816	MX 2004-PA9843	20041008
US 2005165240	A1	20050728	US 2005-508941	20050302
US 7129378	B2	20061031		
US 2006247539	A1	20061221	US 2006-514141	20060901
PRAI US 2002-371158P	P	20020410		
WO 2003-US8827	W	20030407		
US 2005-508941	A1	20050302		

OS MARPAT 139:364424

GI



I

AB A method of preparing amine stereoisomers comprises stereoselectively reducing a sulfinylimine or sulfinylimine stereoisomer that bears on the sulfinyl group a residue of an alc., thiol or amine with a source of a nucleophile to afford

a sulfinylamine stereoisomer, followed by contacting the sulfinylamine stereoisomer with a reagent suitable for the cleavage of a sulfur-nitrogen bond, to afford an amine stereoisomer. The intermediates may also be used in the preparation of sulfoxide and sulfinylamine stereoisomers. Thus, 1-(4-chlorophenyl)cyclobutanecarbonitr ile was treated with Me2CHCH2MgCl and (2S,4R,5S)-4-methyl-5-phenyl-3-tosyl- 1,2,3-oxathiazolidine 2-oxide to give the intermediate imine I which was reduced with NaBH4 in presence of Ti(OEt)4 to give (R)- didesmethylsibutramine, isolated as its D-tartrate.

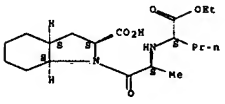
IT 82834-16-0P, Perindopril

RL: SPN (Synthetic preparation); PREP (Preparation); (method of preparing amine stereoisomers via reduction of sulfinylimines in presence of chiral auxiliaries)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L1 ANSWER 132 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:832153 CAPLUS Full-text
DN 139:308016

TI Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril

IN Dubuffet, Thierry; Langlois, Pascal

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1354876	A1	20031022	EP 2003-291420	20030613
EP 1354876	B1	20050427		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 294161	T	20050515	AT 2003-291420	20030613
PT 1354876	T	20050630	PT 2003-291420	20030613
ES 2240921	T3	20051016	ES 2003-291420	20030613
WO 2005003091	A1	20050113	WO 2004-FR1427	20040609
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2003-291420 A 20030613

OS MARPAT 139:308016

AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its alkyl esters, intermediates used in the synthesis of perindopril, were prepared by condensation of 2-(hydroxymethyl)cyclohexanone with glycine benzyl or alkyl ester to give (2RS,3aRS)-3,3a,4,5,6,7-hexahydro-2H-indole-2- carboxylic acid esters, which underwent catalytic hydrogenation of the double bond and resolution using a chiral amine. In an example, (2S,3aS,7aS)-perhydroindole-2-carboxylic acid was prepared with chemical purity 98% and enantiomeric purity 99%.

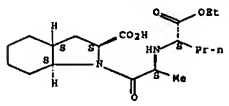
IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PREP (Preparation)
(method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as perindolpril intermediates)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 133 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:832152 CAPLUS Full-text

DN 139:308015

TI Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril

IN Dubuffet, Thierry; Lecouve, Jean-Pierre

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1354875	A1	20031022	EP 2003-291157	20030519
EP 1354875	B1	20041124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 283258	T	20041215	AT 2003-291157	20030519

PT 1354875	T	20050331	PT 2003-291157	20030519
ES 2233914	T3	20050616	ES 2003-291157	20030519
WO 2004103969	A1	20041202	WO 2004-FR1225	20040519

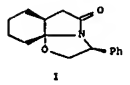
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2003-291157 A 20030519

OS CASREACT 139:308015; MARPAT 139:308015

GI



I

AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its alkyl or benzyl esters, intermediates used in the synthesis of perindopril, were prepared by condensation of (2-oxocyclohexyl)acetic acid with (S)-phenylglycinol to give lactam I, reductive ring opening of the oxazole ring, cleavage of the 2-hydroxy-1-phenylethyl group, reaction with triflic anhydride, cyanation, hydrolysis of the cyano group, and hydrogenation of the double bond. In an example, (2S,3aS,7aS)-perhydroindole-2-carboxylic acid was obtained as the tosylate in enantiomeric purity 99%.

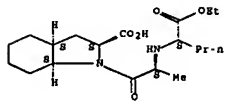
IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PREP (Preparation)
(method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as perindopril intermediates)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 134 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:832151 CAPLUS Full-text

DN 139:308014

TI Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril

IN Dubuffet, Thierry; Langlois, Pascal

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1354874	A1	20031022	EP 2003-290931	20030415
EP 1354874	B1	20041124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AT 283257	T	20041215	AT 2003-290931	20030415
PT 1354874	T	20050331	PT 2003-290931	20030415
ES 2233913	T3	20050616	ES 2003-290931	20030415
WO 2004092133	A1	20041028	WO 2004-FR858	20040407

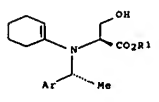
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2003-290931 A 20030415

OS CASREACT 139:308014; MARPAT 139:308014

GI



I

AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its alkyl or benzyl esters, intermediates used in the synthesis of perindopril, were prepared by

condensation of L-serine alkyl or benzyl ester with acetophenone derivs. ArCOMe (Ar = alkylphenyl or naphthyl), reduction of the imine formed, reaction with cyclohexanone to give I, halodehydroxylation, radical cyclization, and deprotection. In an example, (2S,3aS,7aS)-perhydroindole-2-carboxylic acid was obtained with chemical purity 98% and enantiomeric purity 99%.

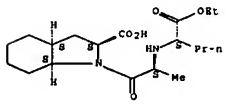
IT 82834-16-0P, Perindopril

RL: PNU (Preparation, unclassified); PREP (Preparation)
(method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as perindopril intermediates)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 135 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2003:832150 CAPLUS Full-text

DN 139:307680

TI Preparation of the L-arginine salt of perindopril and its use as an ACE inhibitor

IN Damien, Gerard; Lefoulon, Francois; Marchand, Bernard

PA Les Laboratoires Servier, Fr.

SO Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1354873	A1	20031022	EP 2003-290383	20030217
EP 1354873	B1	20040714		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
FR 2838648	A1	20031024	FR 2002-4847	20020418
FR 2838648	B1	20040521		
WO 2003087050	A2	20031023	WO 2003-FR507	20030217
WO 2003087050	A3	20040325		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

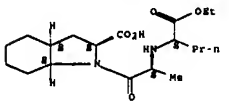
	AU 2003222921	A1	20031027	AU 2003-222921	20030217
	AT 271036	T	20040715	AT 2003-290383	20030217
	PT 1354873	T	20041029	PT 2003-290383	20030217
	ES 2224092	T3	20050301	ES 2003-3290383	20030217
	ZA 2003001395	A	20030902	ZA 2003-1395	20030220
	US 2003199568	A1	20031023	US 2003-371865	20030221
	US 6696481	B2	20040224		
	NO 2003000849	A	20031020	NO 2003-849	20030224
	AU 2003200700	A1	20031106	AU 2003-200700	20030227
	NZ 524478	A	20040528	NZ 2003-524478	20030228
	CN 1451656	A	20031029	CN 2003-107148	20030307
	MX 2003PA02346	A	20050826	MX 2003-PA2346	20030318
	BR 2003000709	A	20040908	BR 2003-709	20030321
	JP 2003321493	A	20031111	JP 2003-83250	20030325
	JP 3737488	B2	20060118		
	CA 2423825	A1	20031018	CA 2003-2423825	20030403
	CA 2423825	C	20060221		
	HK 1057367	A1	20051014	HK 2004-100189	20040110
PRAI	FR 2002-4847	A	20020418		
	WO 2003-FR507	W	20030217		

AB The L-arginine salt of perindopril, which has increased storage stability over the corresponding tert-butylamine salt, is prepared, and its use for the treatment of hypertension and cardiac insufficiencyclaimed.

IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of the L-arginine salt of perindopril and its use as an ACE inhibitor)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



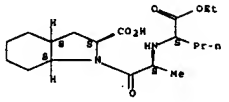
IT 612548-45-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of the L-arginine salt of perindopril and its use as an ACE inhibitor)

RN 612548-45-5 CAPLUS
CN L-Arginine, (2S,3aS,7aS)-1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

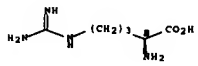
Absolute stereochemistry. Rotation (-).



CM 2

CRN 74-79-3
CMF C6 H14 N4 O2

Absolute stereochemistry.



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 136 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:777526 CAPLUS Full-text
DN 139:286322
TI PAR receptor-mediated antiangiogenic activity of thrombin and use of PAR receptor agonists for the treatment of cancer and other angiogenesis-associatad diseases
IN Sukhatme, Vikas P.; Merchan, Jaime; Chan, Barden
PA Beth Israel Deaconess Medical Center, USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003079978	A2	20031002	WO 2003-US8121	20030314
	WO 2003079978	A3	20040226		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

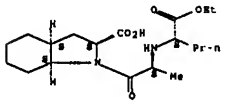
	AU 2003218213	A1	20031008	AU 2003-218213	20030314
	US 2005232925	A1	20051020	US 2005-508317	20050616
PRAI	US 2002-365165P	P	20020318		
	WO 2003-US8121	W	20030314		

AB The present invention features pharmaceutical compns. and methods to inhibit angiogenesis, with implications to cancer therapy. These methods are based on the discovery that activated thrombin has antiangiogenic activity and that this antiangiogenic activity is at least in part, mediated through the activation of a class of thrombin receptors termed, protease-activated receptor (PAR). Pharmaceutical compns. and methods are also directed to a class of proteases which mediate this activation, particularly the urokinase plasminogen activator (uPA) polypeptide.

IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE inhibitor; PAR receptor-mediated antiangiogenic activity of thrombin and use of PAR receptor agonists for treatment of cancer and other angiogenesis-associated diseases)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 137 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:771360 CAPLUS Full-text
DN 139:277168
TI Method for the synthesis of (2S)-indoline-2-carboxylic acid for use in the synthesis of perindopril
IN Souvie, Jean-Claude; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1348684	A1	20031001	EP 2003-290879	20030409
	EP 1348684	B1	20060308		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 319668	T	20060315	AT 2003-290879	20030409
	PT 1348684	T	20060531	PT 2003-290879	20030409

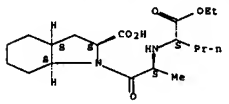
	ES 2260585	T3	20061101	ES 2003-3290879	20030409
	AU 2004230294	A1	20041028	AU 2004-230294	20040407
	CA 2521877	A1	20041028	CA 2004-2521877	20040407
	WO 2004092095	A1	20041028	WO 2004-FR857	20040407
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	BR 2004009095	A	20060411	BR 2004-9095	20040407
	CN 1768019	A	20060503	CN 2004-80009239	20040407
	JP 2006522014	T	20060928	JP 2006-500165	20040407
	IN 2005DN04126	A	20070831	IN 2005-DN4126	20050913
	US 2006183919	A1	20060817	US 2005-552676	20051007
	US 7196204	B2	20070327		
	NO 2005005257	A	20051109	NO 2005-5257	20051109
	US 2007112204	A1	20070517	US 2007-649980	20070105
PRAI	EP 2003-290879	A	20030409		
	WO 2004-FR857	W	20040407		
	US 2005-552676	A3	20051007		

AB (2S)-indoline-2-carboxylic acid, an intermediate used in the synthesis of perindopril, was prepared by resolution of racemic indoline-2-carboxylic acid by reaction with (R)-α-methylbenzylamine. In an example, (2S)-indoline-2-carboxylic acid was obtained with enantiomeric purity > 99.5 %.

IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of (2S)-indoline-2-carboxylic acid via resolution as intermediate in synthesis of perindopril)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

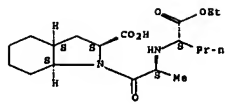
L8 ANSWER 138 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:738076 CAPLUS Full-text
DN 139:250328
TI Compressed tablets based on microcapsules having modified release

IN Jorda, Rafael; Autant, Pierre
PA Flamel Technologies, Fr.
SO Fr. Demande, 46 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI FR 2837100	A1	20030919	FR 2002-3336	20020318
FR 2837100	B1	20040723		
CA 2479057	A1	20030925	CA 2003-2479057	20030314
WO 2003077888	A2	20030925	WO 2003-FR827	20030314
WO 2003077888	A3	20040415		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003242818	A1	20030929	AU 2003-242818	20030314
EP 1485071	A2	20041215	EP 2003-744400	20030314
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008487	A	20050118	BR 2003-8487	20030314
CN 1642530	A	20050720	CN 2003-806302	20030314
JP 2005527522	T	20050915	JP 2003-575941	20030314
IN 2004KN01250	A	20060505	IN 2004-KN1250	20040827
MX 2004PA09010	A	20041126	MX 2004-PA9010	20040915
ZA 2004008412	A	20060830	ZA 2004-8412	20041018
US 2005266078	A1	20051201	US 2005-507886	20050623
PRAI FR 2002-3336	A	20020318		
WO 2003-FR827	W	20030314		

AB Preparation of a prolonged-release compressed tablet comprising a core containing the active principle and a coating which controls the release of active principal is disclosed. Prolonged-release microcapsules cong. metformin hypochloride crystal were prepared A compressed tablet contained. above microcapsules 769.23, mannitol 492.31, Crospovidone 230.77, aspartame 19.23, flavor 16.23, and magnesium stearate 7.69 mg.
IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compressed tablets based on microcapsules having modified release)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



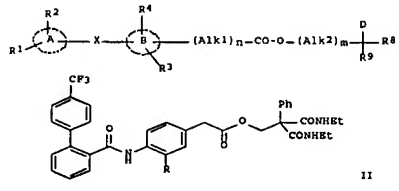
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 139 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:696857 CAPLUS Full-text
DN 139:230479
TI Preparation of [4-(1,1'-biphenyl-2-ylcarbonylamino or benzoylamino)phenyl]acetic acid esters as microsomal triglyceride transfer protein (MTP) inhibitors
IN Hagiwara, Atsushi; Oe, Yasuhiro; Odani, Naoya; Watanabe, Shizue; Ikenogami, Taku; Kawai, Takashi; Madono, Kenya; Taniguchi, Toshio
PA Japan Tobacco Inc., Japan
SO PCT Int. Appl., 561 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

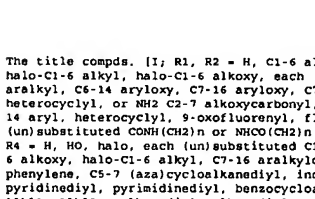
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003072532	A1	20030904	WO 2003-JP2398	20030228
W: AE, AG, AL, AM, AU, AZ, BA, BB, BR, BY, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, ID, IL, IN, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, RU, SC, SG, TJ, TM, TN, TT, UA, US, UZ, VC, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2460682	A1	20030904	CA 2003-2460682	20030228
AU 2003211617	A1	20030909	AU 2003-211617	20030228
JP 2003321424	A	20031111	JP 2003-53869	20030228
JP 3662566	B2	20050622		
BR 2003006292	A	20040824	BR 2003-6292	20030228
EP 1479666	A1	20041124	EP 2003-743078	20030228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1630629	A	20050622	CN 2003-804734	20030228
ZA 2005002495	A	20050920	ZA 2005-2495	20030228
ZA 2005002496	A	20051012	ZA 2005-2496	20030228
NZ 531890	A	20060224	NZ 2003-531890	20030228
RU 2293721	C2	20070220	RU 2004-124370	20030228
CN 1943786	A	20070411	CN 2006-10099709	20030228
NZ 543229	A	20070531	NZ 2003-543229	20030228
MX 2004PA02602	A	20040811	MX 2004-PA2602	20040319
ZA 2004002275	A	20050423	ZA 2004-2275	20040323
IN 2004KN00460	A	20060324	IN 2004-KN460	20040407
NO 2004001872	A	20040506	NO 2004-1872	20040506
US 2005075367	A1	20050407	US 2004-492831	20041008

JP 2005194281	A	20050721	JP 2005-19579	20050127
JP 2005220132	A	20050818	JP 2005-19739	20050127
JP 2005220133	A	20050818	JP 2005-20179	20050127
AU 2005248950	A1	20060119	AU 2005-248950	20051223
IN 2007KN00581	A	20070706	IN 2007-KN581	20070216
PRAI JP 2002-53876	A	20020228		
AU 2003-211617	A3	20030228		
CN 2003-804734	A3	20030228		
JP 2003-53869	A3	20030228		
NZ 2003-531890	A3	20030228		
WO 2003-JP2398	W	20030228		
IN 2004-KN460	A3	20040407		

OS MARPAT 139:230479
GI



I

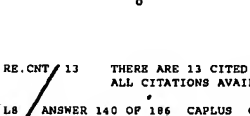


II

AB The title compds. [I; R1, R2 = H, C1-6 alkyl, C3-7 cycloalkyl, C1-6 alkoxy, halo-C1-6 alkyl, halo-C1-6 alkoxy, each (un)substituted C6-14 aryl, C7-16 aralkyl, C6-14 aryloxy, C7-16 aryloxy, C7-16 aralkyloxy, C7-15 arylcarbonyl, heterocyclyl, or NH2 C2-7 alkoxycarbonyl, halo, C2-6 alkenyl; the ring A = C6-14 aryl, heterocyclyl, 9-oxofluorenyl, fluorenyl; X = CO2(CH2)n, each N-(un)substituted CONH(CH2)n or NHCO(CH2)n (wherein n = an integer of 0-3); R3, R4 = H, HO, halo, each (un)substituted C1-6 alkyl, heterocyclyl, or CONH2, C1-6 alkoxy, halo-C1-6 alkyl, C7-16 aralkyloxy, C1-6 acyl; the ring B = phenylene, C5-7 (aza)cycloalkanediyl, indoledi yl, benzimidazolediyl, pyridinediyl, pyrimidinediyl, benzocycloalkanedi yl, quinolinediyl, etc.; Alk11, Alk12 = alkanediyl, alkenediyl; n, m = 0-3; D = C1-6 alkyl, C2-6 alkenyl, C2-7 alkoxycarbonyl, NR42COR43 (wherein R42 = H, C1-6 alkyl; R43 = C4-14 aryl, C7-16 aralkyl), etc.; R8, R9 = H, C1-6 alkyl, (un)substituted C6-14 aryl, CONH2, or NH2, succinimid-2-yl, hydroxy-C1-6 alkyl, CO2H or its ester, (CH2)sO2CR20 (wherein R20 = H, C1-6 alkyl, C3-7 cycloalkyl; s = 0-3)] or prodrugs thereof or pharmaceutically acceptable salts of either are prepared These compds. I electively inhibit microsomal triglyceride transfer protein (MTP) of small intestine, are metabolized in blood or liver, and residual amount of MTP inhibitors is small enough not to substantially inhibit liver MTP and hence causes no side effects such as a fatty liver. They are useful for prevention or treatment of hyperlipidemia, arteriosclerosis, coronary artery diseases, obesity, diabetes, or hypertension. Thus, 519 mg 4-[(4'-trifluoromethyl-1,1'-biphenyl-2-ylcarbonyl)amino]phenylacetic acid (preparation given), 317 mg 2-hydroxymethyl-2-phenylmalonic acid diethylamide

pg, and 268 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride were dissolved in 5 mL CH2Cl2 and stirred at room temperature for 6 h to give, after distillation of the solvent and silica gel chromatog., 725 mg 4-[(4'-trifluoromethyl-1,1'-biphenyl-2-ylcarbonyl)amino]phenylacetic acid 2,2-bis(ethylcarbamoyl)-2-phenylethyl ester (II; R = H). II (R = H) and II (R = Me) inhibited the triglyceride transport between liposomes by MTP with IC50 of 0.6 and 0.39 nM, resp., and the secretion of apolipoprotein B from HepG2 cell with IC50 of 0.65 and 0.46, resp. Pharmaceutical formulations, e.g. a tablet containing 2-[[2-[4-[(4'-trifluoromethyl-1,1'- biphenyl-2-ylcarbonyl)amino]-3-(pyrrolidinocarbonyl)phenyl]acetoxy]methyl]- 2-phenylmalonic acid di-Et ester, were described.
IT 82834-16-0, Perindopril
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antihypertensive agent, coadministration drugs containing; preparation of [(biphenylylcarbonylamino or benzoylamino)phenyl]acetic acid esters as microsomal triglyceride transfer protein (MTP) inhibitors for treatment or prevention of diseases)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 140 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:678514 CAPLUS Full-text
DN 139:191440
TI Methods of treating or preventing a cardiovascular condition using a cyclooxygenase-1 inhibitor
IN Kruk, Elaine S.
PA USA
SO U.S. Pat. Appl. Publ., 32 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003162824	A1	20030828	US 2002-292255	20021112
PRAI US 2001-331346P	P	20011112		
US 2001-338291P	P	20011113		

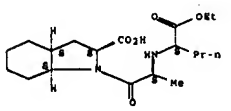
OS MARPAT 139:191440
AB Methods for treating or preventing one or more cardiovascular conditions in a subject comprises treating the subject with a therapeutically effective amount

of a selective cyclooxygenase-1 inhibitor or a pharmaceutically-acceptable salt, tautomer or prodrug thereof alone or in combination with either a drug used in the treatment or prevention of a cardiovascular condition or a non-drug therapy used in the treatment of a cardiovascular condition. Cyclooxygenase-1 inhibitor, 5-(4-Chlorophenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)pyrasole (I), was prepared from 4'-chloroacetophenone and (4-methoxyphenyl)hydrazine hydrochloride. I inhibited development of atherosclerosis in cholesterol-fed apoE knockout mice.

IT 82834-16-0, Perindopril
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiotensin converting enzyme inhibitor; cyclooxygenase-1 inhibitor for treating or preventing cardiovascular conditions)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

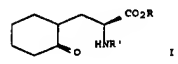


RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

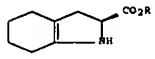
CN 1753869	A	20060329	CN 2004-80005407	20040227
JP 2006519175	T	20060824	JP 2006-500161	20040227
US 2006167273	A1	20060727	US 2005-546967	20050824
US 7157484	B2	20070102		
PRAI EP 2003-290487	A	20030228		
WO 2004-FR444	A	20040227		

OS CASREACT 139:197771; MARPAT 139:197771

GI



I



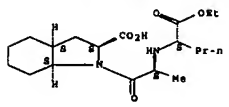
II

AB (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and its benzyl or alkyl esters were prepared by reaction of 1-(1-cyclohexen-1-yl)pyrrolidine with (R)-ICH2CH(NR')CO2R (R is H, benzyl, or alkyl; R' is an amine-protecting group) to afford cyclohexanone derivs. I. Cyclization of I, e.g., using p-toluenesulfonic acid, gave compds. II, which underwent catalytic hydrogenation to afford compds. of the invention. The title acid was obtained in 87% yield and 99% enantiomeric purity by this method.

IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(method for synthesis of perhydroindolecarboxylic acid and esters as perindopril intermediates)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



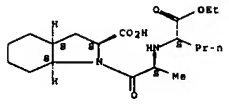
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 142 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:670106 CAPLUS Full-text
DN 139:321745
TI The ACE Gene I/D Polymorphism Is Not Associated With the Blood Pressure and Cardiovascular Benefits of ACE Inhibition
AU Hartley, Stephen B.; Tzourio, Christophe; Cambien, Francois; Poirier, Odette; Raoux, Segolene; Chalmers, John; Chapman, Neil; Colman, Samuel; Leguennec, Solenn; MacMahon, Stephen; Neal, Bruce; Ohkubo, Takayoshi; Woodward, Mark
CS Department of Physiology, University of Melbourne, Melbourne, Australia
SO Hypertension (2003), 42(3), 297-303
CODEN: HPRTDN; ISSN: 0194-911X
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB The insertion/deletion (I/D) polymorphism of the angiotensin-converting enzyme (ACE) gene might have consequences for the risks of vascular diseases. We examined the ACE genotype and the effects of a perindopril-based blood pressure-lowering regimen on macrovascular events, dementia, and cognitive decline among hypertensive and nonhypertensive patients with a history of cerebrovascular disease. ACE I/D genotypes were measured in 5688 of 6105 individuals with previous stroke or transient ischemic attack who participated in the PROGRESS trial. The DD genotype was significantly (P<0.0001) less frequent in Asian subjects (Chinese and Japanese, 14.7%) than in non-Asian subjects (32.0%). Controlling for racial background, there were no assocns. between ACE genotypes and cerebrovascular disease history or cardiovascular risk factors, including baseline blood pressure. The ACE genotype was not associated with the long-term risks of stroke, cardiac events, mortality, dementia, or cognitive decline; neither did the ACE genotype predict the blood pressure reduction associated with the use of the ACE inhibitor perindopril. Similarly, there was no evidence that the ACE genotype modified the relative benefits of ACE inhibitor-based therapy over placebo. This study provides no evidence that in patients with cerebrovascular disease, knowledge of ACE genotype is useful for predicting either the risk of disease or the benefits of perindopril-based blood pressure-lowering treatment.

IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE genotype and effects of perindopril based blood pressure lowering regimen on macrovascular events, dementia and cognitive decline among hypertensive and nonhypertensive patients with a history of cerebrovascular disease)

RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 143 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:609507 CAPLUS Full-text
DN 139:149930
TI Process for the preparation of high purity perindopril and intermediates useful in its synthesis
IN Simig, Gyula; Mezei, Tibor; Porcs-Makkay, Marta; Mandi, Attila
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1333026	A1	20030806	EP 2002-290206	20020130
EP 1333026	B1	20070627		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 365714	T	20070715	AT 2002-290206	20020130
IN 2003MU00069	A	20050128	IN 2003-MU69	20030117
CA 2474003	A1	20030807	CA 2003-2474003	20030129
WO 2003064388	A2	20030807	WO 2003-IB691	20030129
WO 2003064388	A3	20040205		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 2003000231	A2	20030828	HU 2003-231	20030129
EE 200400107	A	20041015	EE 2004-107	20030129
BR 2003007293	A	20041221	BR 2003-7293	20030129
CN 1622936	A	20050601	CN 2003-802714	20030129
JP 2005521667	T	20050721	JP 2003-564011	20030129
NZ 534168	A	20061130	NZ 2003-534168	20030129
AP 1741	A	20070630	AP 2004-3091	20030129
US 2005119492	A1	20050602	US 2004-503272	20040729
MX 2004PA07444	A	20050617	MX 2004-PA7444	20040730
NO 2004003472	A	20040820	NO 2004-3472	20040820
BG 108858	A	20050531	BG 2004-108858	20040827
HK 1076101	A1	20070518	HK 2005-108134	20050916

	US 2007197821	A1	20070823	US 2007-788454	20070420
	US 7279595	B2	20071009		
PRAI	EP 2002-290206	A	20020130		
	WO 2003-IB691	W	20030129		
	US 2004-503272	A3	20040729		

OS MARPAT 139:149930

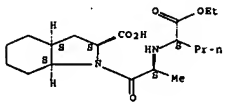
AB The invention relates to 1-[2(S)-[1(S)-(ethoxycarbonyl)butylamino]propiony l]-(3aS,7aS)octahydroindole-2(S)-carboxylic acid (perindopril) and its tert-butylamine salt, free of contaminants derivable from dicyclohexylcarbodiimide, and a process for their synthesis. The invention also relates to N-[1-(ethoxycarbonyl)butyl]-N- (alkoxycarbonyl)alanine intermediates used in the synthesis of perindopril, a known ACE inhibitor. Thus, N-[1-(ethoxycarbonyl)butyl]-N- (ethoxycarbonyl)alanine, prepared by ethoxycarbonylation of N-[1-(ethoxycarbonyl)butyl]alanine, was treated with thionyl chloride in CH2Cl2 and acylated by perhydroindole-2-carboxylic acid in THF at reflux for 4-4.5 h. The product was treated with tert-butylamine to afford 55% perindopril eburmine.

IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril eburmine
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of high purity perindopril and intermediates useful in its synthesis)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



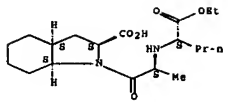
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 144 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:509921 CAPLUS Full-text
DN 139:69148
TI Method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril
IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

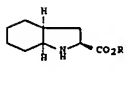
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1323729	A1	20030702	EP 2003-290607	20030312
	EP 1323729	B1	20041103		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 281465	T	20041115	AT 2003-290607	20030312
	PT 1323729	T	20050228	PT 2003-290607	20030312
	ES 2231760	T3	20050516	ES 2003-290607	20030312
	WO 2004083237	A1	20040930	WO 2004-FR592	20040312
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,				

ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2003-290607 A 20030312

OS CASREACT 139:69148; MARPAT 139:69148

GI



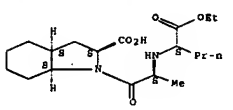
AB Title compds. I [R = H, CH2Ph, alkyl] were prepared by treating 2,7-oxepanedione with XCH2CH(NHR2)CO2R1 [R1 = CH2Ph, alkyl; R2 = protective group] to give HO2C(CH2)4COCH2CH(NH2)CO2R1 which was cyclized to the lactam, cyclized to the indole with Ti, and reduced over Pt, Pd, Rh, or Ni catalyst. Thus, I [R = H] was prepared from 2,7-oxepanedione and (2S)-ICH2CH(NHCO2CMe3)CO2CH2Ph in 5 steps.

IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(method for synthesis of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid and esters as intermediates in the synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 145 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:488613 CAPLUS Full-text
DN 139:22503
TI Method for the synthesis of perindopril and its pharmaceutically-acceptable salts
IN Dubuffet, Thierry; Lecouve, Jean-pierre
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DT Patent
LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1321471	A1	20030625	EP 2003-290605	20030312
	EP 1321471	B1	20050504		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 294814	T	20050515	AT 2003-290605	20030312
	PT 1321471	T	20050729	PT 2003-290605	20030312
	ES 2240919	T3	20051016	ES 2003-290605	20030312
	WO 2004083238	A1	20040930	WO 2004-FR594	20040312
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI EP 2003-290605 A 20030312

OS CASREACT 139:22503; MARPAT 139:22503

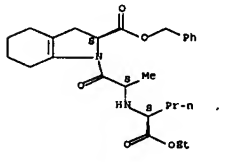
AB Perindopril and its pharmaceutically-acceptable salts were prepared from 2,7-oxepanedione by a multistep procedure, i.e., reaction with (R)-XCH2CH(NHBoc)CO2CH2Ph (X is Br or iodo; Boc is tert-butoxycarbonyl), cyclization of deprotected 2-amino-4-oxononanedioic acid derivative, Ti-catalyzed coupling to form the indole ring system, reaction with N-[(S)-1-carbethoxybutyl]-(S)-alanine, and catalytic hydrogenation. In an example, perindopril was obtained with enantiomeric purity 99%.

IT 539820-43-4P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for synthesis of perindopril and its pharmaceutically-acceptable salts)

RN 539820-43-4 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]-2,3,4,5,6,7-hexahydro-, phenylmethyl ester, (2S)- (9CI) (CA INDEX NAME)

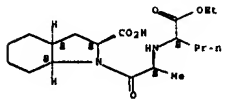
Absolute stereochemistry.



IT 82834-16-0P, Perindopril 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(Preparation)
(method for synthesis of perindopril and its pharmaceutically-acceptable salts)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

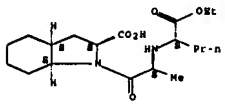


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

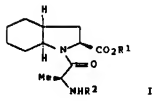
CRN 75-64-9
CMF C4 H11 N

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 146 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:470308 CAPLUS Full-text
DN 139:22502
TI Method for the synthesis of (2S,3aS,7aS)-1-[(S)-alanyl]octahydro-1H-indole-2-carboxylic acid derivatives for use in the synthesis of perindopril
IN Dubuffet, Thierry; Lecouve, Jean-Pierre
PA Les Laboratoires Servier, Fr.
SO Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1319668	A1	20030618	EP 2003-290606	20030312
	EP 1319668	B1	20041027		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	AT 280775	T	20041115	AT 2003-290606	20030312
	PT 1319668	T	20050228	PT 2003-290606	20030312
	ES 2231759	T3	20050516	ES 2003-290606	20030312
	WO 2004082357	A2	20040930	WO 2004-FR593	20040312
	WO 2004082357	A3	20041028		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GM, ML, MR, NE, SN, TD, TG				
PRAI	EP 2003-290606	A	20030312		

OS CASREACT 139:22502; MARPAT 139:22502
GI

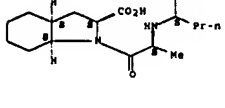


I

AB Alanyloctahydroindolecarboxylic acid derivs. I (R1 is H, alkyl, or benzyl; R2 is a protecting group) were prepared from 2,7-oxepanedione by a multistep procedure, i.e., reaction with (R)-XCH2CH(NHR3)CO2R4 (X is Br or iodo; R3 is a

protecting group; R4 is benzyl or alkyl), cyclization of deprotected 2-amino-4-oxononanedioic acid derivative, Ti-catalyzed coupling to form the indole ring system, reaction with an alanine deriv., and catalytic hydrogenation. In an example, I (R1 = H, R2 = tert-butoxycarbonyl) was obtained with enantiomeric purity 99%.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of alanyloctahydroindolecarboxylic acid deriv. for use in synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 147 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:77804 CAPLUS Full-text
DN 138:107004
TI A process for the preparation of perindopril, its analogs and salts using 2,5-dioxooxazolidine intermediate compounds
IN Cid, Pau
PA Adir, Pr.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

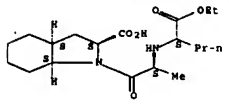
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1279665	A2	20030129	EP 2002-16262	20020723
	EP 1279665	A3	20030312		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	IN 2002MU00639	A	20040417	IN 2002-MU639	20020712
	WO 2003010142	A2	20030206	WO 2002-EP8223	20020723
	WO 2003010142	A3	20030828		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				

FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GM, ML, MR, NE, SN, TD, TG

	AU 2002328954	A1	20030217	AU 2002-328954	20020723
	AU 2002328954	B2	20071004		
	HU 2002002414	A2	20030228	HU 2002-2414	20020723
	BR 2002011422	A	20040817	BR 2002-11422	20020723
	CN 1529694	A	20040915	CN 2002-814322	20020723
	JP 2005501829	T	20050120	JP 2003-515501	20020723
	NZ 530578	A	20070223	NZ 2002-530578	20020723
	ZA 2004000323	A	20050117	ZA 2004-323	20040115
	MX 2004PA00649	A	20041027	MX 2004-PA649	20040121
	US 2004248814	A1	20041209	US 2004-484672	20040712
	IN 2005MU00042	A	20070824	IN 2005-MU42	20050114
PRAI	EP 2001-500197	A	20010724		
	WO 2002-EP8223	W	20020723		

OS MARPAT 138:107004
AB Perindopril {(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid} or its analogs or salts were prepared by treating RcCH(CO2Ra)NHCHRbCO2H (Ra, Rb = C1-4 alkyl, Rc = C1-6alkyl) with X2C:O (X is a leaving group) to give a 2,5-dioxooxazolidine, which reacts with octahydro-1H-indole-2-carboxylic acid or ester to give the desired product. In an example, N,N'-carbonyldiimidazole was added to a suspension of N-[(S)-1- carbethoxybutyl]-(S)-alanine in CH2Cl2 and the mixture kept at 0° for 1 h. (2S,3aS,7aS)-octahydroindole-2-carboxylic acid was added at -5°C and the solution kept at this temperature for 1 h to give 80% perindopril (isolated as the tert-butylamine salt).
IT 82834-16-0P, Perindopril 107133-36-8P, Perindopril erbumine
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of perindopril using dioxooxazolidine intermediate)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

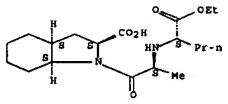


RN 107133-36-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

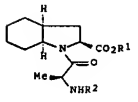
L8 ANSWER 148 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:866690 CAPLUS Full-text
DN 137:353317
TI Method for synthesis of (2S,3aS,7aS)-1-(S)-alanyloctahydro-1H-indole-2-carboxylic acid derivatives as intermediates for synthesis of perindopril
IN Mezei, Tibor; Porcs-Makkay, Marta; Simig, Gyula
PA Les Laboratoires Servier S.A., Fr.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1256590	A1	20021113	EP 2002-291853	20020723
EP 1256590	B1	20060301		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
FR 2827860	A1	20030131	FR 2001-9839	20010724
FR 2827860	B1	20041210		
IN 2002MU00629	A	20040417	IN 2002-MU629	20020711
CA 2455706	A1	20030227	CA 2002-2455706	20020723
WO 2003016336	A1	20030227	WO 2002-FR2627	20020723
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

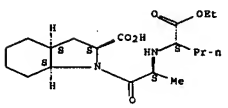
AU 2002334027	A1	20030303	AU 2002-334027	20020723
BR 2002011334	A	20040928	BR 2002-11334	20020723
CN 1533398	A	20040929	CN 2002-814609	20020723
JP 2005500386	T	20050106	JP 2003-521258	20020723
JP 3868957	B2	20070117		
NZ 530427	A	20050826	NZ 2002-530427	20020723
AT 318838	T	20060315	AT 2002-291853	20020723
PT 1256590	T	20060630	PT 2002-291853	20020723
ES 2259071	T3	20060916	ES 2002-2291853	20020723
HU 2002002437	A2	20030228	HU 2002-2437	20020724
ZA 2004000246	A	20060726	ZA 2004-246	20040113
MX 2004PA00443	A	20040318	MX 2004-PA443	20040115
US 2004198988	A1	20041007	US 2004-484022	20040115
US 7060842	B2	20060613		
PRAI FR 2001-9839	A	20010724		
WO 2002-FR2627	W	20020723		

OS CASREACT 137:353317
GI



AB Alanyloctahydroindolecarboxylic acid derivs. I (R1 = H, alkyl, benzyl; R2 is a protecting group) were prepared as intermediates for the synthesis of perindopril. Thus, treatment of Me (2S)-2,3-dihydro-1H-indole-2- carboxylate with Boc-L-Ala-OH (Boc = tert-butoxycarbonyl) in THF in the presence of Et3N and DCC for 6 h at room temperature afforded 81% Me (2S)-1-[(2S)-2-[(tert-butoxycarbonyl)amino]propionyl]-2,3-dihydro-1H- indole-2-carboxylate, which was hydrogenated over Pd/C at 60°C to give 90% I (R1 = Me, R2 = Boc).
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of alanyloctahydroindolecarboxylic acid derivs. as intermediates for synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

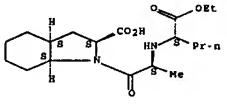
L8 ANSWER 149 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:754995 CAPLUS Full-text
DN 137:268473
TI Porous drug matrices and methods of manufacture thereof
IN Straub, Julia; Altreuter, David; Bernstein, Howard; Chickering, Donald E.; Khattak, Sarwat; Randall, Greg
PA Acusphere Inc., USA
SO U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U. S. 6,395,300.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002142050	A1	20021003	US 2002-53929	20020122
US 6395300	B1	20020528	US 1999-433486	19991104
EP 1642572	A1	20060405	EP 2005-27194	20000525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
CN 1823737	A	20060830	CN 2005-10136940	20000525
US 6645528	B1	20031111	US 2000-694407	20001023
US 6932983	B1	20050823	US 2000-706045	20001103
ZA 2001010347	A	20030730	ZA 2001-10347	20011218
US 2005048116	A1	20050303	US 2004-924642	20040824
US 2005058710	A1	20050317	US 2004-928886	20040827
PRAI US 1999-136323P	P	19990527		
US 1999-158659P	P	19991008		
US 1999-433486	A2	19991104		
US 2000-186310P	P	20000302		
CN 2000-808161	A3	20000525		
EP 2000-939365	A3	20000525		
US 2002-53929	A3	20020122		

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solution and hydrophilic or hydrophobic excipients that stabilize the drug and inhibit crystallization, and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. Hydrophobic or hydrophilic excipients may be selected to stabilize the drug in crystalline form by inhibiting crystal growth or to stabilize the drug in amorphous form by preventing crystallization The pore forming agent can be either a volatile

liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Thus, 5.46 g of PEG 8000, 0.545 g of prednisone, and 0.055 g of Span 40 were dissolved in 182 mL of methylene chloride. A solution of 3.27 g of ammonium bicarbonate in 18.2 mL of water was added to the organic solution (phase ratio 1:10) and homogenized for 5 min at 16,000 RPM. The resulting emulsion was spray dried on a benchtop spray dryer using an air-atomizing nozzle and nitrogen as the drying gas.
IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(porous drug matrixes and methods of manufacture thereof)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 150 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:574955 CAPLUS Full-text
DN 137:129203
TI Combinations of azetidinone sterol absorption inhibitor(s) with cardiovascular agent(s) for the treatment of vascular conditions
IN Kosoglou, Teddy; Ress, Rudyard Joseph; Strony, John; Veltri, Enrico P.; Hauer, William
PA Schering Corporation, USA
SO PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 12

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002058731	A2	20020801	WO 2002-US1196	20020125
WO 2002058731	A3	20031120		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UZ, VN, YU, ZA, ZM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,				

GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2434436	A1	20020801	CA 2002-2434436	20020125
CA 2562982	A1	20020801	CA 2002-2562982	20020125
CA 2563051	A1	20020801	CA 2002-2563051	20020125
AU 2002241903	A1	20020806	AU 2002-241903	20020125
US 2003069221	A1	20030410	US 2002-57339	20020125
EP 1385548	A2	20040204	EP 2002-707500	20020125
EP 1385548	B1	20070523		
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BR 2002006644	A	20040225	BR 2002-6644	20020125
HU 2003003923	A2	20040301	HU 2003-3923	20020125
EP 1413331	A2	20040428	EP 2004-161	20020125
EP 1413331	A3	20040630		
EP 1413331	B1	20071003		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517919	T	20040617	JP 2002-559065	20020125
CN 1582168	A	20050216	CN 2002-804219	20020125
EP 1541175	A2	20050615	EP 2005-3029	20020125
EP 1541175	A3	20060412		
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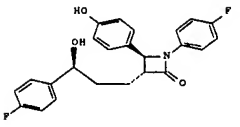
EP 1671650	A1	20060621	EP 2006-5831	20020125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1915429	A	20070221	CN 2006-10126233	20020125
EP 1785144	A2	20070516	EP 2007-3151	20020125
EP 1785144	A3	20070523		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI				
AT 362757	T	20070615	AT 2002-707500	20020125
EP 1810693	A2	20070725	EP 2007-9475	20020125
EP 1810693	A3	20071017		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, AL, LT, LV, MK, RO, SI				
NZ 545332	A	20070928	NZ 2002-545332	20020125
ZA 2003005692	A	20041025	ZA 2003-5692	20030723
ZA 2003005694	A	20041025	ZA 2003-5694	20030723
ZA 2003005693	A	20050209	ZA 2003-5693	20030723
IN 2003CN01150	A	20050422	IN 2003-CN1150	20030724
NO 2003003358	A	20030912	NO 2003-3358	20030725
MX 2003PA06724	A	20031024	MX 2003-PA6724	20030725
US 2004097482	A1	20040520	US 2003-639900	20030813
HK 1060854	A1	20070907	HK 2004-103917	20040601
US 2005153952	A1	20050714	US 2004-998400	20041129
US 2006198793	A1	20060907	US 2005-158429	20050622
IN 2006CN01141	A	20070831	IN 2006-CN1141	20060403
AU 2007201970	A1	20070524	AU 2007-201970	20070503
JP 2007211031	A	20070823	JP 2007-141163	20070528
PRAI US 2001-264275P	P	20010126		
US 2001-264396P	P	20010126		
US 2001-264600P	P	20010126		
US 2001-323842P	P	20010921		
US 2001-323839P	P	20010921		
US 2001-324123P	P	20010921		
CA 2002-2434682	A3	20020125		
CN 2002-807208	A3	20020125		
EP 2002-704233	A3	20020125		

EP 2002-705933	A3	20020125	
EP 2002-707500	A3	20020125	
EP 2002-707556	A3	20020125	
EP 2002-714773	A3	20020125	
JP 2002-559066	A3	20020125	
US 2002-57323	A3	20020125	
US 2002-57646	A1	20020125	
WO 2002-US1196	W	20020125	
US 2002-136968	A3	20020501	
IN 2003-CN1150	A3	20030724	
AU 2006-202618	A3	20060620	

OS MARPAT 137:129903

GI



I

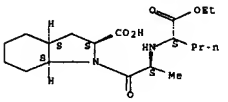
AB The present invention provides compns., therapeutic combinations and methods including: (a) at least one sterol absorption inhibitor and (b) at least one cardiovascular agent different from the sterol absorption inhibitor, which can be useful for treating vascular conditions, obesity, diabetes and lowering plasma levels of sterols. Tablets were prepared containing cardiovascular agents which can be coadministered with formulations containing, e.g., I. The preparation of I was given.

IT 82834-16-0, Perindopril 107133-36-8, Perindopril erbumine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combinations of azetidinone sterol absorption inhibitor(s) with cardiovascular agent(s) for the treatment of vascular conditions)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



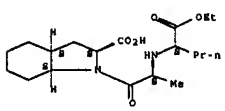
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L4 ANSWER 161 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:851113 CAPLUS Full-text

DN 135:371632

TI Preparation of the ACE-inhibiting β-crystalline form of perindopril tert-butylamine salt and antihypertensive pharmaceutical formulation containing it

IN Pfeiffer, Bruno; Ginot, Yves-Michel; Coquerel, Gerard; Beilles, Stephane

PA Adir et Compagnie, Fr.

SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001087836	A1	20011122	WO 2001-FR2168	20010706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

FR 2811319	A1	20020111	FR 2000-8792	20000706
FR 2811319	B1	20020823		
HU 2001002813	A2	20020328	HU 2001-2813	20010705
HU 2001002813	A3	20031229		
CA 2415442	A1	20011122	CA 2001-2415442	20010706
EP 1294689	A1	20030326	EP 2001-954059	20010706
EP 1294689	B1	20060426		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012244	A	20030624	BR 2001-12244	20010706
JP 2003533508	T	20031111	JP 2001-584233	20010706
JP 3592297	B2	20041124		
EE 200300002	A	20040816	EE 2003-2	20010706
NZ 523234	A	20050128	NZ 2001-523234	20010706
AP 1407	A	20050530	AP 2002-2710	20010706
AT 324367	T	20060515	AT 2001-954059	20010706
EP 1676839	A2	20060705	EP 2006-75789	20010706
EP 1676839	A3	20061108		
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PT 1294689	T	20060731	PT 2001-954059	20010706
ES 2262666	T3	20061201	ES 2001-1954059	20010706
IN 2002MU00594	A	20040417	IN 2002-MU594	20020703
MX 2002PA12921	A	20040730	MX 2002-PA12921	20021219
IN 2002MN01845	A	20050204	IN 2002-MN1845	20021219
US 2004029813	A1	20040212	US 2002-312902	20021231
ZA 2003000024	A	20040205	ZA 2003-24	20030102
NO 2003000050	A	20030106	NO 2003-50	20030106
NO 323446	B1	20070507		
BG 107533	A	20031128	BG 2003-107533	20030205
HR 2003000079	A1	20030430	HR 2003-79	20030206
JP 2005002121	A	20050106	JP 2004-206159	20040713
US 2005203165	A1	20050915	US 2005-52489	20050204
US 7259181	B2	20070821		
IN 2005MU00265	A	20070330	IN 2005-MU265	20050310
SG 125974	A1	20061030	SG 2005-1529	20050311
IN 2005MN00575	A	20051007	IN 2005-MN575	20050607
AU 2006235841	A1	20061123	AU 2006-235841	20061103
PRAI FR 2000-8792	A	20000706		
AU 2001-276419	A3	20010706		
EP 2001-954059	A3	20010706		
JP 2001-584233	A3	20010706		
WO 2001-FR2168	W	20010706		
IN 2002-MU594	A3	20020703		
IN 2002-MN1845	A3	20021219		
US 2002-312902	B1	20021231		

AB The more-stable β-crystalline form of the tert-butylamine salt of perindopril (I), characterized by its X-ray powder diffraction pattern, is prepared by refluxing the tert-butylamine salt of perindopril in dichloromethane, followed by cooling the mixture, and filtration. A I-contg tablet formulation is presented.

IT 107133-36-8
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(preparation of the ACE-inhibiting β-crystalline form of perindopril tert-butylamine salt and antihypertensive pharmaceutical formulation containing it)

RN 107133-36-8 CAPLUS

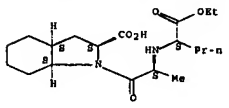
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 152 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:851112 CAPLUS Full-text

DN 135:371631

TI Preparation and X-ray characterization of the ACE-inhibiting α-crystalline form of the tert-butylamine salt of perindopril

IN Pfeiffer, Bruno; Ginot, Yves-Michel; Coquerel, Gerard; Beilles, Stephane

PA Les Laboratoires Servier, Fr.

SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001087835	A1	20011122	WO 2001-FR2167	20010706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2811320	A1	20020111	FR 2000-8793	20000706
FR 2811320	B1	20020823		
CA 2415438	A1	20011122	CA 2001-2415438	20010706
EP 1296947	A1	20030402	EP 2001-954058	20010706
EP 1296947	B1	20040204		
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BR 2001012367	A	20030513	BR 2001-12367	20010706
JP 2003533507	T	20031111	JP 2001-584232	20010706
JP 3602826	B2	20041215		
AT 258918	T	20040215	AT 2001-954058	20010706
NZ 523173	A	20040430	NZ 2001-523173	20010706
PT 1296947	T	20040531	PT 2001-954058	20010706
EE 200300001	A	20040816	EE 2003-1	20010706
ES 2214434	T3	20040916	ES 2001-1954058	20010706
AP 1537	A	20060228	AP 2002-2691	20010706
W: GM, GH, KE, LS, MW, MZ, SL, SD, SZ, TZ, UG, ZW				
CZ 297672	B6	20070228	CZ 2003-357	20010706
SK 285714	B6	20070607	SK 2003-149	20010706
IN 2002MU00597	A	20040417	IN 2002-MU597	20020703
ZA 2002010092	A	20031212	ZA 2002-10092	20021212
IN 2002MN01815	A	20050204	IN 2002-MN1815	20021216
MX 2002PA12949	A	20030515	MX 2002-PA12949	20021219
US 2003186896	A1	20031002	US 2002-312961	20021231
NO 2003000024	A	20030103	NO 2003-24	20030103
NO 323447	B1	20070507		
BG 107532	A	20031231	BG 2003-107532	20030205
BG 64868	B1	20060731		
HR 2003000077	A1	20030430	HR 2003-77	20030206
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JP 2005047902	A	20050224	JP 2004-206158	20040713
IN 2004MN00628	A	20060707	IN 2004-MN628	20041104
IN 2005MU00129	A	20060901	IN 2005-MU129	20050208
SG 125975	A1	20061030	SG 2005-1530	20050311
AU 2006101079	A5	20070118	AU 2006-101079	20061222
AU 2007203451	A1	20070816	AU 2007-203451	20070725
PRAI FR 2000-8793	A	20000706		
JP 2001-584232	A3	20010706		
WO 2001-FR2167	W	20010706		
IN 2002-MU597	A3	20020703		
IN 2002-MN1815	A3	20021216		
US 2002-312961	B1	20021231		

AB The α-crystalline form of the ACE-inhibiting tert-butylamine salt of perindopril (I) is prepared by refluxing the tert-butylamine salt of perindopril in Et acetate, cooling the mixture, and filtering the I α- crystal modification, which is characterized by its powder X-ray diffraction pattern, and a I-containing pharmaceutical formulation is prepared

IT 107133-36-8, Perindopril erbumine
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(preparation and X-ray characterization of the ACE-inhibiting α-crystalline form of the tert-butylamine salt of perindopril)

RN 107133-36-8 CAPLUS

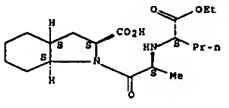
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 153 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2001:816626 CAPLUS Full-text

DN 135:344373

TI Process for preparing the novel γ crystalline form of the diuretic perindopril tert-butylamine salt

IN Pfeiffer, Bruno; Ginot, Yves-Michel; Coquerel, Gerard; Beilles, Stephane

PA Adir et Compagnie, Fr.

SO PCT Int. Appl., 11 pp.
CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001083439	A2	20011108	WO 2001-FR2169	20010706

WO 2001083439	A3	20020207		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2811318	A1	20020111	FR 2000-8791	20000706
FR 2811318	B1	20020823		
CA 2415447	A1	20011108	CA 2001-2415447	20010706
AU 200176420	A	20011112	AU 2001-76420	20010706
EP 1296948	A2	20030402	EP 2001-954060	20010706
EP 1296948	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012211	A	20030506	BR 2001-12211	20010706
AT 249435	T	20030915	AT 2001-954060	20010706
JP 2003531890	T	20031028	JP 2001-580868	20010706
JP 3592296	B2	20041124		
PT 1296948	T	20031231	PT 2001-954060	20010706
ES 2206423	T3	20040516	ES 2001-1954060	20010706
NZ 523311	A	20040625	NZ 2001-523311	20010706
EE 200300003	A	20040816	EE 2003-3	20010706
AP 1452	A	20050930	AP 2002-2709	20010706
W: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW				
IN 2002MU00593	A	20040417	IN 2002-MU593	20020703
MX 2002PA12904	A	20030922	MX 2002-PA12904	20021219
IN 2002MN01893	A	20050204	IN 2002-MN1893	20021230
US 2003158121	A1	20030821	US 2002-312903	20021231
ZA 2003000025	A	20040210	ZA 2003-25	20030102
NO 2003000051	A	20030106	NO 2003-51	20030106
NO 323445	B1	20070507		
BG 107534	A	20031231	BG 2003-107534	20030205
HR 2003000078	A1	20030430	HR 2003-78	20030206
HR 2003000078	B1	20040630		
US 2004248817	A1	20041209	US 2004-811727	20040329
JP 2005002120	A	20050106	JP 2004-206157	20040713
SG 125976	A1	20061030	SG 2005-1531	20050311
IN 2005MN00362	A	20050923	IN 2005-MN362	20050502
PRAI FR 2000-8791	A	20000706		
JP 2001-580868	A3	20010706		
WO 2001-FR2169	W	20010706		
IN 2002-MN1893	A3	20021230		
US 2002-312903	B1	20021231		

AB The γ crystalline form of the diuretic perindopril tert-butylamine salt (I) is prepared by refluxing a chloroform-I solution, cooling the solution to 0°, and filtering the I γ crystal modification which is characterized by its X- ray diffraction pattern; a I-containing formulation is presented.

IT 107133-36-8
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(process for preparing the novel γ crystalline form of the diuretic perindopril tert-butylamine salt)

RN 107133-36-8 CAPLUS

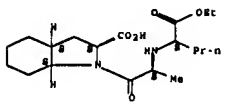
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd.

with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

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	HU 2001001336	A3	20030328		
	CA 2405486	A1	20010816	CA 2001-2405486	20010405
	AU 200148470	A	20010820	AU 2001-48470	20010405
	EP 1268424	A1	20030102	EP 2001-921486	20010405
	EP 1268424	B1	20070808		
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	BR 2001009836	A	20030624	BR 2001-9836	20010405
	JP 2003531825	T	20031028	JP 2001-558419	20010405
	JP 3939553	B2	20070704		
	NZ 521454	A	20040326	NZ 2001-521454	20010405
	EE 200200575	A	20040415	EE 2002-575	20010405
	AP 1385	A	20050408	AP 2002-2630	20010405
	AT 369338	T	20070815	AT 2001-921486	20010405
	IN 2002MU00598	A	20040417	IN 2002-MU598	20020703
	ZA 2002007419	A	20030916	ZA 2002-7419	20020916
	IN 2002MN01284	A	20040703	IN 2002-MN1284	20020918
	US 2003069431	A1	20030410	US 2002-239129	20020919
	US 6835843	B2	20041228		
	MX 2002PA09706	A	20040906	MX 2002-PA9706	20021002
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	NO 324174	B1	20070903		
	BG 107249	A	20030731	BG 2002-107249	20021104
	HK 1053309	A1	20070511	HK 2003-105542	20030801
PRAI	FR 2000-4379	A	20000406		
	WO 2001-FR1026	W	20010405		

OS CASREACT 135:167034

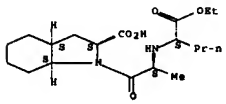
AB Perindopril [(2S,3aS,7aS)-1-[(2S)-2-[(1S)-1-(ethoxycarbonyl)butylamino]propionyl]octahydro-1H-indole-2-carboxylic acid] was prepared by coupling (2S,3aS,7aS)octahydroindole-2-carboxylic acid tosylate with N-[(S)-1-carbethoxybutyl]-(S)-alanine, followed by catalytic hydrogenation to remove the benzyl group. In an example, the coupling reaction was carried out in Et acetate in the presence of Et3N, 1-hydroxybenzotriazole and dicyclohexylcarbodiimide at 30° for 3h to give 92% perindopril benzyl ester.

IT 82834-16-0P, Perindopril
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 107133-36-8P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(method for synthesis of perindopril)

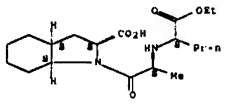
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

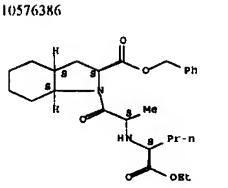
CRN 75-64-9
CMF C4 H11 N

IT 122454-52-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for synthesis of perindopril)

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 165 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:581830 CAPLUS Full-text
DN 135:137713
TI Synthesis of N-[(S)-1-carboxybutyl]-(S)-alanine esters for synthesis of perindopril
IN Souvie, Jean-Claude; Renaud, Alain
PA Adir et Compagnie, Fr.
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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	HU 2001001337	A3	20021128		
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	EP 1272454	B1	20070523		
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	AP 1417	A	20050524	AP 2002-2639	20010410
	AT 362913	T	20070615	AT 2001-923776	20010410
	IN 2002MU00595	A	20040417	IN 2002-MU595	20020703

	ZA 2002007689	A	20030925	ZA 2002-7689	20020925
	IN 2002MN01352	A	20040703	IN 2002-MN1352	20020930
	NO 2002004811	A	20021004	NO 2002-4811	20021004
	MX 2002PA09888	A	20040906	MX 2002-PA9888	20021007
	US 2003109743	A1	20030612	US 2002-257239	20021009
	US 6774259	B2	20040810		
	BG 107250	A	20030630	BG 2002-107250	20021104
	HK 1053300	A1	20050401	HK 2003-105540	20030801
PRAI	FR 2000-4610	A	20000411		
	WO 2001-FR1088	W	20010410		

OS CASREACT 135:137713; MARPAT 135:137713

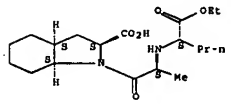
AB Title alanine derivs. (S)-RO2CCHPr-L-Ala-OH (R = C1-C6 alkyl) were prepared by condensation of L-alanine with PrCOCO2R under hydrogen pressure and 5% Pd/C as catalyst. In an example, hydrogenation of a mixture of 25 kg L-alanine, 1.1 kg soda and 36 kg Et 2-oxopentanoate in H2O over 5% Pd/C at room temperature and 1 bar pressure afforded N-[(S)-1-carbethoxybutyl]-(S)- alanine.

IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of [carboxybutyl]alanine esters for synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

LB ANSWER 156 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:581647 CAPLUS Full-text
DN 135:137711
TI Synthesis of N-[(S)-1-carboxybutyl]-(S)-alanine esters for synthesis of perindopril
IN Souvie, Jean-Claude
PA Adir et Compagnie, Fr.
SO PCT Int. Appl., 8 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001056353	A2	20010809	WO 2001-FR959	20010330
	WO 2001056353	A3	20020418		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,				

	HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2807037	A1	20011005	FR 2000-4112	20000331
	FR 2807037	B1	20020510		
	CA 2404700	A1	20010809	CA 2001-2404700	20010330
	CA 2404700	C	20070220		
	AU 200148433	A	20010814	AU 2001-48433	20010330
	HU 2001001335	A2	20011128	HU 2001-1335	20010330
	HU 2001001335	A3	20021128		
	EP 1268398	A2	20030102	EP 2001-921440	20010330
	EP 1268398	B1	20050608		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2003534241	T	20031118	JP 2001-556065	20010330
	JP 3930322	B2	20070613		
	BR 2001009609	A	20040113	BR 2001-9609	20010330
	NZ 521324	A	20040326	NZ 2001-521324	20010330
	EE 200200553	A	20040415	EE 2002-553	20010330
	AU 2001248433	B2	20041028	AU 2001-248433	20010330
	AT 297377	T	20050615	AT 2001-921440	20010330
	PT 1268398	T	20050930	PT 2001-921440	20010330
	ES 2242743	T3	20051116	ES 2001-1921440	20010330
	AP 1483	A	20051231	AP 2002-2628	20010330
	W: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW				
	IN 2002MU00596	A	20040417	IN 2002-MU596	20020703
	ZA 2002007150	A	20030905	ZA 2002-7150	20020905
	IN 2002MN01255	A	20040626	IN 2002-MN1255	20020913
	US 2003045744	A1	20030306	US 2002-221973	20020916
	US 6818788	B2	20041116		
	MX 2002PA09378	A	20030212	MX 2002-PA9378	20020925
	NO 2002004616	A	20020926	NO 2002-4616	20020926
	BG 107234	A	20030731	BG 2002-107234	20021030
	HK 1053301	A1	20050318	HK 2003-105541	20030801
PRAI	FR 2000-4112	A	20000331		
	WO 2001-FR959	W	20010330		

OS CASREACT 135:137711; MARPAT 135:137711

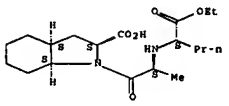
AB Title alanine derivs. (S)-RO2CCHPr-L-Ala-OH (R = C1-C6 alkyl) were prepared by condensation of sodium pyruvate with (S)-RO2CCHPrNH2.HCl under hydrogen pressure and 5% Pd/C as catalyst. In an example, hydrogenation of a mixture of 3 kg (S)-Et norvalinate hydrochloride and 2 kg sodium pyruvate in NaOH aqueous solution over 5% Pd/C at 35° and 1.2 bar pressure afforded 62% N-[(S)-1-carbethoxybutyl]-(S)-alanine.

IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of (carboxybutyl)alanine esters for synthesis of perindopril)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LB ANSWER 157 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:338762 CAPLUS Full-text
DN 134:362292
TI Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
IN Farr, Spencer
PA Phase-1 Molecular Toxicology, USA
SO PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001032928	A2	20010510	WO 2000-US30474	20001103
	WO 2001032928	A3	20020725		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 1999-165398P	P	19991105		
	US 2000-196571P	P	20000411		

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

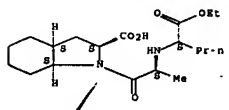
IT 82834-16-0, Perindopril
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BIOL (Biological study)
(methods of determining individual hypersensitivity to a pharmaceutical agent
from gene expression profile)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LB ANSWER 158 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2001:137173 CAPLUS Full-text
DN 134:178396
TI Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
IN Del Soldato, Piero
PA Nicox S.A., Fr.
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001012584	A2	20010222	WO 2000-EP7225	20000727
	WO 2001012584	A3	20020829		
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	IT 99MI1817	A1	20010212	IT 1999-MI1817	19990812
	CA 2381409	A1	20010222	CA 2000-2381409	20000727
	BR 2000013264	A	20020416	BR 2000-13264	20000727
	EP 1252133	A2	20021030	EP 2000-953102	20000727
	EP 1252133	B1	20050608		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	HU 2002003939	A2	20030328	HU 2002-3939	20000727
	JP 2003515526	T	20030507	JP 2001-516885	20000727
	CN 1433396	A	20030730	CN 2000-814049	20000727
	NZ 516889	A	20041029	NZ 2000-516889	20000727
	AU 781643	B2	20050602	AU 2000-65670	20000727
	AT 297375	T	20050615	AT 2000-953102	20000727

EP 1593664	A1	20051109	EP 2005-104064	20000727	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY					
RU 2264383	C2	20051120	RU 2002-103509	20000727	
ES 2243292	T3	20051201	ES 2000-953102	20000727	
NZ 535559	A	20051223	NZ 2000-535559	20000727	
CN 1923797	A	20070307	CN 2006-10136231	20000727	
ZA 2002000624	A	20030423	ZA 2002-624	20020123	
US 7186753	B1	20070306	US 2002-48469	20020207	
NO 2002000623	A	20020409	NO 2002-623	20020208	
MX 2002PA01519	A	20020702	MX 2002-PA1519	20020211	
AU 2005203824	A1	20050721	AU 2005-203824	20050628	
IN 2006CN01908	A	20070608	IN 2006-CN1908	20060530	
US 2007197499	A1	20070823	US 2006-642783	20061221	
PRAI IT 1999-MI1817	A	19990812			
CN 2000-814049	A3	20000727			
EP 2000-953102	A3	20000727			
IN 2002-CN187	A3	20000727			
WO 2000-EP7225	W	20000727			
US 2002-48469	A1	20020207			

OS MARPAT 134:178396

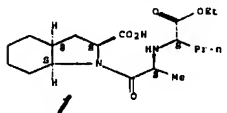
AB Compds. or their salts of general formula (I); A-B-N(O)s wherein: s is an integer equal to 1 or 2; A = R-T1-, wherein R is the drug radical and T1 = (CO)t or (X)t', wherein X = O, S, NR1c, R1c is H or a linear or branched alkyl or a free valence, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1; B = -TB -X2-O- wherein TB = (CO) when t = 0, TB = X when t' = 0, X being as above defined; X2, bivalent radical, is such that the precursor drug of A and the precursor of B meet resp. the pharmacol. tests described in the description. Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(ACE-inhibitor; synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 159 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:742057 CAPLUS Full-text
DN 133:309791

TI Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
IN Del Soldato, Piero
PA Nicox S.A., Fr.
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000061541	A2	20001019	WO 2000-EP3239	20000411
WO 2000061541	A3	20010927		
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DM, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1311923	B1	20020320	IT 1999-MI752	19990413
CA 2370425	A1	20001019	CA 2000-2370425	20000411
BR 2000009703	A	20020108	BR 2000-9703	20000411
EP 1169298	A2	20020109	EP 2000-926870	20000411
EP 1169298	B1	20060104		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY				
JP 2002541236	T	20021203	JP 2000-610818	20000411
TR 200102928	T2	20021223	TR 2001-2928	20000411
HU 2002000714	A2	20021228	HU 2002-714	20000411
NZ 514270	A	20040227	NZ 2000-514270	20000411
RU 2237057	C2	20040927	RU 2001-127574	20000411
AU 777579	B2	20041021	AU 2000-45474	20000411
AT 315021	T	20060215	AT 2000-926870	20000411
PT 1169298	T	20060531	PT 2000-926870	20000411
ES 2256001	T3	20060716	ES 2000-926870	20000411
PL 193919	B1	20070430	PL 2000-350967	20000411
ZA 2001008126	A	20030403	ZA 2001-8126	20011003
MX 2001PA10213	A	20020918	MX 2001-PA10213	20011009
NO 2001004928	A	20011213	NO 2001-4928	20011010
US 6987120	B1	20060117	US 2001-926322	20011015
US 2006030605	A1	20060209	US 2005-234084	20050926
PRAI IT 1999-MI752	A	19990413		
WO 2000-EP3239	W	20000411		
US 2001-926322	A3	20011015		

OS MARPAT 133:309791

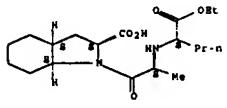
AB Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(ACE-inhibitor; synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 160 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:742053 CAPLUS Full-text
DN 133:310142
TI Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
IN Del Soldato, Piero
PA Nicox S.A., Fr.
SO PCT Int. Appl., 159 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000061537	A2	20001019	WO 2000-EP3234	20000411
WO 2000061537	A3	20010927		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1311924	B1	20020320	IT 1999-MI753	19990413
CA 2370412	A1	20001019	CA 2000-2370412	20000411
BR 2000009702	A	20020108	BR 2000-9702	20000411
EP 1169294	A2	20020109	EP 2000-925203	20000411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541233	T	20021203	JP 2000-610814	20000411
HU 2002003378	A2	20030128	HU 2002-3378	20000411
NZ 514267	A	20040625	NZ 2000-514267	20000411
RU 2237657	C2	20041010	RU 2001-127576	20000411
AU 778989	B2	20041223	AU 2000-44001	20000411
ZA 2001008127	A	20030103	ZA 2001-8127	20011003
MX 2001PA10210	A	20020918	MX 2001-PA10210	20011009
NO 2001004927	A	20011213	NO 2001-4927	20011010
US 6869974	B1	20050322	US 2001-926326	20011015
US 2005261242	A1	20051124	US 2004-24857	20041230
PRAI IT 1999-MI753	A	19990413		
WO 2000-EP3234	W	20000411		
US 2001-926326	A3	20011015		

OS MARPAT 133:310142

AB Compds. A-B-C-N(O)s and A-C1[N(O)s]-B1 or their salts [s is an integer 1 or 2, preferably s = 2; A is the radical of a drug and is such as to meet the

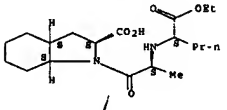
pharmacol. tests reported in the description; C and C1 are two bivalent radicals; the precursors of the radicals B and B1 are such as to meet the pharmacol. test reported in the description] were prepared for use as pharmaceuticals. Thus, (S,S)-N-acetyl-S-(6-methoxy-α-methyl-2-naphthalenylacetyl)cysteine 4-nitroxybutyl ester was prepared (NCX 2101) from naproxene and N-acetylcysteine in the first of 28 synthetic examples given. Pharmacol. test examples and tabular data are also given.

IT 82824-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(drug precursor)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 161 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:628026 CAPLUS Full-text
DN 133:227793
TI Combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease
IN Alexander, John C.; Roniker, Barbara; Desai, Subhash
PA G.D. Searle and Co., USA
SO PCT Int. Appl., 212 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000051642	A1	20000908	WO 2000-US5633	20000303
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2364169	A1	20000908	CA 2000-2364169	20000303
EP 1165136	A1	20020102	EP 2000-912174	20000303
EP 1165136	B1	20030910		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

TR 200102581	T2	20020422	TR 2001-2581	20000303
BR 2000008781	A	20020702	BR 2000-8781	20000303
HU 2002000519	A2	20020729	HU 2002-519	20000303
JP 2002538172	T	20021112	JP 2000-602308	20000303
AT 249242	T	20030915	AT 2000-912174	20000303
EP 1382351	A1	20040121	EP 2003-19610	20000303
EP 1382351	B1	20051123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PT 1165136	T	20040227	PT 2000-912174	20000303
ES 2206204	T3	20040516	ES 2000-912174	20000303
NZ 514205	A	20040730	NZ 2000-514205	20000303
AU 778559	B2	20041209	AU 2000-33945	20000303
AT 310537	T	20051215	AT 2003-19610	20000303
ES 2250803	T3	20060416	ES 2003-3019610	20000303
MX 2001PA09035	A	20040812	MX 2001-PA9035	20010905
IN 2001CN01238	A	20050304	IN 2001-CN1238	20010905
ZA 2001007779	A	20021220	ZA 2001-7779	20010920
HK 1042252	A1	20040423	HK 2002-104154	20020531
US 2004077611	A1	20040422	US 2003-440691	20030519
US 2005250748	A1	20051110	US 2003-637070	20030806
NZ 529635	A	20031219	NZ 2003-529635	20031119
HK 1061200	A1	20060224	HK 2004-104294	20040614
AU 2005201045	A1	20050407	AU 2005-201045	20050309
PRAI US 1999-122977P	P	19990305		
US 1999-122978P	P	19990305		
EP 2000-912174	A3	20000303		
US 2000-518854	B1	20000303		
US 2000-518855	B1	20000303		
WO 2000-US5633	W	20000303		

AB Combinations of an ACE inhibitor and an epoxy-steroidal aldosterone receptor antagonist are described for use in treatment of circulatory disorders. Of particular interest are therapies using epoxy-steroidal-type aldosterone receptor antagonist compds., such as eplerenone, in combination with an angiotensin converting enzyme inhibitor. This co-therapy would be particularly useful to treat congestive heart failure while avoiding or reducing aldosterone-antagonist- induced side effects such as hyperkalemia. Capsules were prepared containing captopril 62.0 and eplerenone 12.5 mg/capsule.

IT 182176-83-6, S 5590
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(S 5590; combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease)

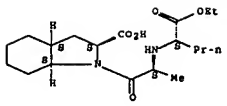
RN 182176-83-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, mixt. with 3-(aminosulfonyl)-4-chloro-N-(2,3-dihydro-2-methyl-1H-indol-1-yl)benzamide (CA INDEX NAME)

CM 1

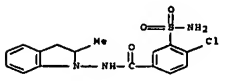
CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 26807-65-8
CMF C16 H16 Cl N3 O3 S

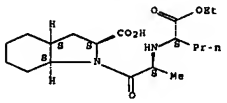


IT 82834-16-0, Perindopril
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy of angiotensin converting enzyme inhibitor and epoxy-steroidal aldosterone antagonist for treatment of cardiovascular disease)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 162 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:191639 CAPLUS Full-text
DN 133:68211
TI Does Chinese ethnicity affect the pharmacokinetics and pharmacodynamics of angiotensin-converting enzyme inhibitors?
AU Ding, P. Y. A.; Hu, O. Yoa-Pu; Pool, P. E.; Liao, W.-C.

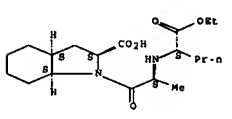
CS Department of Internal Medicine, Veterans General Hospital-Taipei, Taipei, Taiwan
SO Journal of Human Hypertension (2000), 14(3), 163-170
CODEN: JHHYEN; ISSN: 0950-9240
PB Nature Publishing Group
DT Journal; General Review
LA English
AB A review with 53 refs. Information from clin. and pharmacokinetic studies of angiotensin-converting enzyme inhibitors (ACEIs) has come from subjects who are mostly male and Caucasian, but the use of ACEIs extends to populations worldwide. Significant differences between Chinese in general and male Caucasians have been demonstrated in the pharmacokinetics/dynamics of other drug classes, and this could have implications for the use of ACEIs in the Chinese population. These include: significant Chinese/Caucasian genetic variation in the renin-angiotensin system based on an insertion/deletion polymorphism of the ACE gene; the genetic regulation of plasma ACE activity in the Chinese population; and genetic factors involving hypertension which may also influence the response to treatment. Oral and i.v. pharmacokinetic data from various studies of Chinese and Caucasian subjects are available for cilazapril, fosinopril, and perindopril, and pharmacodynamic data are available for eight different ACEIs. Based on these data, there are few differences in the pharmacokinetics of ACEIs between Chinese and Caucasians. Most ACEIs showed good blood-pressure-lowering efficacy in Chinese (benazepril, enalapril, fosinopril and spirapril), with perhaps less efficacy of cilazapril or a relatively shorter-term effect with cilazapril or perindopril, compared to Caucasions. Chinese experience more cough from ACEIs (captopril and enalapril) than Caucasians. Data suggest that fosinopril may not induce cough in as many subjects as do other ACEIs, and this seems to be true of Chinese as well. The mechanism, currently unknown, could involve fosinopril's dual elimination pathway (hepatic and renal). Pharmacokinetic data also support the use of fosinopril in congestive heart failure where elimination pathways may be impaired. In conclusion, ethnic differences between Chinese and Caucasians with respect to ACE and angiotensin gene polymorphism, which might be expected to differentially affect the action of ACEIs in these two ethnic groups, do not, in fact, have such an effect. Rather, differences among the ACEIs appear to be more important.

IT 82834-16-0, Perindopril
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Chinese ethnicity effect on the pharmacokinetics and pharmacodynamics of angiotensin-converting enzyme inhibitors)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

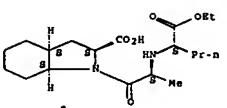
Absolute stereochemistry. Rotation (-).



RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 163 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:599960 CAPLUS Full-text
DN 131:199561
TI Synthetic routes of perindopril
AU Chen, Ying-Wu; Chen, Jing
CS Wuhan College of Chemical Technology, Wuhan, 430074, Peop. Rep. China
SO Zhongguo Yiyao Gongye Zazhi (1999), 30(8), 382-384
CODEN: ZYGZEA; ISSN: 1001-8255
PB Zhongguo Yiyao Gongye Zazhi Bianjibu
DT Journal; General Review
LA Chinese
AB A brief review, with 16 refs., illustrating synthetic schemes for the preparation of perindopril.
IT 82834-16-0P, Perindopril
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(review of synthesis of perindopril)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L10 ANSWER 164 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:34890 CAPLUS Full-text
DN 130:100648
TI ACE inhibitor nitric acid salts
IN Del Soldato, Piero
PA Nicox S.A., Fr.
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9900361	A1	19990107	WO 1998-EP3946	19980624
W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,				

CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2292794	A1	19990107	CA 1998-2292794	19980624
AU 9887300	A	19990119	AU 1998-87300	19980624
AU 740411	B2	20011101		
EP 1019370	A1	20000719	EP 1998-938668	19980624
EP 1019370	B1	20030102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO				
HU 2000003133	A2	20010328	HU 2000-3133	19980624
HU 2000003133	A3	20021028		
JP 2002506456	T	20020226	JP 1999-505294	19980624
RU 2194037	C2	20021210	RU 2000-100825	19980624
AT 230393	T	20030115	AT 1998-938668	19980624
ES 2190095	T3	20030716	ES 1998-938668	19980624
IL 132691	A	20040601	IL 1998-132691	19980624
BR 9810459	A	20061003	BR 1998-10459	19980624
US 6218417	B1	20010417	US 1999-423287	19991108
PRAI IT 1997-MI1523	A	19970627		
WO 1998-EP3946	W	19980624		

OS MARPAT 130:100648

AB The invention relates to products having an improved antihypertensive activity and fewer side effects, in particular in the bronchi. Nitric acid salts of ACE inhibitors show an antihypertensive activity combined with platelet-antiaggregating activity. I.p. injection of enalapril nitrate at 100 or 300 μg/kg to rats with induced hypertension inhibited the symptoms by 35 and 67 %, vs. 18 and 55 % for enalapril maleate.

IT 219553-93-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE inhibitor nitric acid salts with improved antihypertensive effects)

RN 219553-93-2 CAPLUS

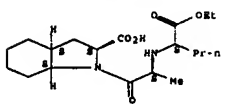
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, mononitrate (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 7697-37-2

CMF H N O3

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 165 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1998:438838 CAPLUS Full-text

DN 129:174067

TI Possible participation of angiotensin-converting enzyme and of leukocyte elastase in pathogenesis of non-insulin dependent diabetes mellitus

AU Dotsenko, V. L.; Demidova, T. Yu.; Neshkova, E. A.; Ametov, A. S.; Yarovaya, G. A.

CS Ross. Med. Aked. Posldiplomn. Obrazovaniya, Moscow, 123836, Russia

SO Voprosy Meditsinskoi Khimii (1998), 44(2), 203-212
CODEN: VMDKAM; ISSN: 0042-8809

PB NII Biomeditsinskoi Khimii

DT Journal

LA Russian

AB It is commonly accepted that the tolerance to insulin and hyperglycemia of the patients with non-insulin dependent diabetes mellitus (NIDDM) is due to some defect of insulin receptors or disturbances in the signaling pathway of the cell. This disease is often eccompanied by hypertension. In this peper the high activity of plasma kallikrein-kinin system (KKS) (kallikrein activity was 6-8-fold higher then normal), of angiotensin-converting enzyme (ACE) (4-fold greater than normal), and of leukocyte elastase (2.7-fold higher than normel) were demonstrated in plasma of patients with NIDDM. Increased KKS activity was coincident with rising ACE activity, which may be the cause of the fast bradykinin inactivation and onset of hypertension. The treatment with ACE inhibitor during 3 mo (4 mg of Perindopril per day) decreased ACE activity in patients' plasma which was accompanied by decreased arterial pressure and some restoration of carbohydrate metebolism indicators. The hyperinsulinemic euglycemic clamping of 7 patients with NIDDM and essentiel hypertension showed that ACE-inhibitor (Perindopril, 4 mg) prevented bradykinin from destruction and increased the glucose consumption by tissues. The high activity of polymorphonuclear leukocytes and secretion of the elastase in NIDDM patients' plasma and/or instability of plasma and granular membranes of leukocytes in conditions of hyperglycemic plasma are probably the cause of endothelial irritation and high ACE secretion. Secondly, the leukocyte may be the cause of injury and decreased susceptibility of cell receptors for insulin and bradykinin.

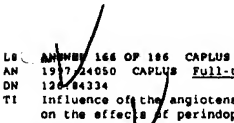
IT 82834-16-0, Perindopril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(participation of angiotensin-converting enzyme and of leukocyte elastase in pathogenesis of non-insulin dependent diabetes mellitus)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 166 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1997:24050 CAPLUS Full-text

DN 126:84334

TI Influence of the angiotensin II type 1 receptor gene polymorphism on the effects of perindopril and nitrendipine on arterial stiffness in hypertensive individuals

AU Benetos, Athanase; Cambien, Francois; Gautier, Sylvie; Ricard, Sylvain; Safar, Michel; Laurent, Stephane; Lacolley, Patrick; Poirier, Odette; Topouchian, Jirar; Asmar, Roland

CS Broussais Hospital, Institut National de la Sante et de la Recherche Medicale, Paris, 75014, Fr.

SO Hypertension (Dallas) (1996), 28(6), 1081-1084
CODEN: HPRTDN; ISSN: 0194-911X

PB American Heart Association

DT Journal

LA English

AB Angiotensin-converting enzyme inhibitors improve arterial stiffness independently of blood pressure reduction Since the authors have recently shown that in hypertensive individuals the A 1166C polymorphism of the engiotensin II type 1 receptor (AT1-R) is an independent determinant of aortic stiffness, the euthors designed the present study to assess the influence of this polymorphism on the changes of aortic stiffness after chronic treatment with the angiotensin-converting enzyme inhibitor perindopril and the calcium channel blocker nitrendipine. Forty perindopril- and 42 nitrendipine-treated hypertensive individuals were studied. The authors evaluated aortic stiffness by measuring the carotid-femoral pulse wave velocity. Carriers of the AT1-R C allele showed higher baseline values of pulse wave velocity than AA homozygotes. In the perindopril group, e threefold greater reduction in pulse wave velocity was observed in carriers of the C allele then in AA homozygotes (-2.85 vs. -0.94 m/s, resp.), whereas in the nitrendipine group, pulse wave velocity decreased only in AA homozygotes and not in AT1-R C carriers (-1.38 vs. +0.04 m/s, resp.). These results indicate that according to the AT1-R A 1166C genotype, an angiotensin-converting enzyme inhibitor and a calcium channel blocker affect pulse wave velocity in opposite ways. Since some evidence shows that increased pulse wave velocity may enhance cardiovascular risk, it might be useful for physicians to consider the AT1-R genotype when prescribing an engiotensin-converting enzyme inhibitor or calcium channel blocker to a hypertensive individual.

IT 82834-16-0, Perindopril

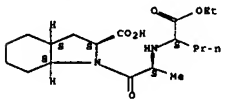
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(influence of angiotensin II type 1 receptor gene polymorphism on effects of perindopril and nitrendipine on arterial stiffness in hypertensive humans)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 167 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1995:858706 CAPLUS Full-text

DN 123:266119

TI A pharmaceutical product comprising a salicylate of an esterifieble ACE inhibitor

IN Byrne, William; Rynne, Andrew

PA Cal International Ltd., Ire.

SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2

DT Patent

LA English

PAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9520571	A1	19950803	WO 1995-IE12	19950127
W: AT, AU, BR, CA, CH, CN, DE, DK, ES, FI, GB, HU, JP, LU, NL, NO, PL, RO, RU, SE, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IE, LU, SE, NE				
CA 2182198	A1	19950803	CA 1995-2182198	19950127
AU 9516709	A	19950815	AU 1995-16709	19950127
EP 741699	A1	19961113	EP 1995-908364	19950127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
GB 2300635	A	19961113	GB 1996-16297	19950127
GB 2300635	B	19980617		
JP 09509150	T	19970916	JP 1995-519969	19950127
ZA 9500703	A	19950929	ZA 1995-703	19950130
US 5852047	A	19981222	US 1996-682663	19960729
PRAI IE 1994-80	A	19940128		
WO 1995-IE12	A	19950127		

AB Salicylates of esterifiable ACE inhibitors, especially captropril-5-aspirinate, and processes for their preparation ere described. A pharmaceutical composition (e.g. capsules or tablets) contains the compds. of the invention and may also contain a diuretic and K+ salts.

IT 82834-16-0, Perindopril

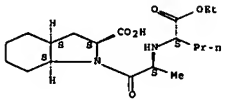
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of compns. containing salicylate of esterifiable ACE-inhibitors)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA

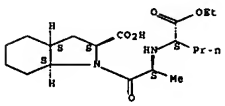
INDEX NAME)

Absolute stereochemistry. Rotation (-).

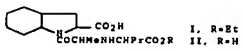


IT 82834-16-0D, Perindopril, aspirin deriva.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of compns. containing salicylate of esterifiable ACE-inhibitors)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 168 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1993:73362 CAPLUS Full-text
DN 118:73362
TI Synthesis and ACE inhibitory activity of the stereoisomers of perindopril (S 9490) and perindoprilate (S 9780)
AU Vincent, Michel; Marchand, Bernard; Remond, Georges; Jaguelin-Guinamant, Sylvie; Damien, Gerard; Portevin, Bernard; Baumal, Jean Yves; Volland, Jean Paul; Bouchet, Jean Paul; et al.
CS Inst. Rech. Serv. 11, Suresnes, 92150, Fr.
SO Drug Design and Discovery (1992), 9(1), 11-28
CODEN: DDDIEV; ISSN: 1055-9612
DT Journal
LA English
GI

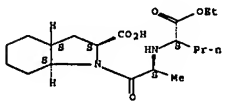


I, R=Et
II, R=H

AB Preindopril, a powerful ACE (angiotensin converting enzyme) inhibitor contains 5 chiral carbons, and thus there is the possibility of 25 = 32 stereoisomers for the general structure I. These 32 stereoisomers were prepared by crosscoupling the 8 stereoisomers of benzyl perhydroindole-2- carboxylate with the 4 stereoisomers of 2-(1-carbethoxybutylamino)propioni c acid, and hydrogenating the resulting benzyl esters. Each stereoisomer of perindopril furnished by saponification of the corresponding diacid stereoisomer (II) of perindoprilate which is the active form of perindopril. For each of the 32 stereoisomers of II, the in vitro ACE inhibitory potency was determined Four of them, including perindoprilate, had activities in the nanomolar range, and 4 more were ca. 10-fold less active. The 4 acid esters of I corresponding resp. to the 4 most active diacids II, in vitro were studied (1 mg/kg via the oral route) for their in vivo activity in dogs. The oral absorption of the active acid esters I and their activation to the active diacid II depended only on the chiralities of the 2 ring junction carbons of the perhydroindole ring.

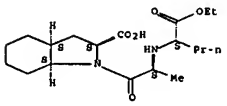
IT 82834-16-0DP, Perindopril, isomers 82834-16-0P
145513-30-0P 145513-31-1P 145513-32-2P
145513-33-3P 145513-34-4P 145513-35-5P
145513-36-6P 145513-37-7P 145513-38-8P
145513-39-9P 145513-40-2P 145513-41-3P
145513-42-4P 145513-43-5P 145513-44-6P
145513-45-7P 145513-46-8P 145513-47-9P
145513-48-0P 145513-49-1P 145513-50-4P
145513-51-5P 145513-52-6P 145513-53-7P
145513-54-8P 145513-55-9P 145513-56-0P
145513-57-1P 145513-58-2P 145513-59-3P
145513-94-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and angiotensin I-converting enzyme inhibitory activity of, chirality-structure activity in relation to)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



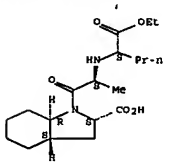
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



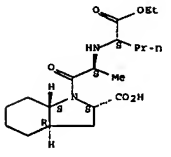
RN 145513-30-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aβ,7aα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



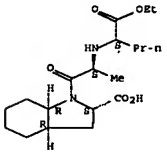
RN 145513-31-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aα,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



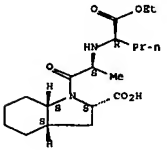
RN 145513-32-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(R*)],2α,3aα,7aα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



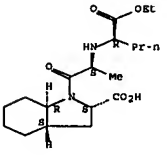
RN 145513-33-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



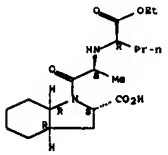
RN 145513-34-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3aβ,7aα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



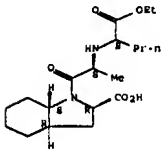
RN 145513-35-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3aα,7aα]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



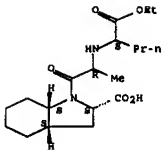
RN 145513-36-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



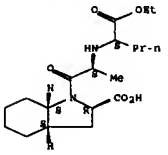
RN 145513-37-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2α,3aβ,7aβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



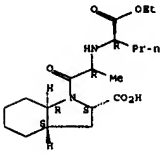
RN 145513-38-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2α,3aα,7aα]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 145513-39-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(S*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

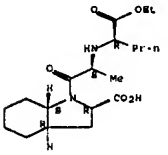
Absolute stereochemistry.



RN 145513-40-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-

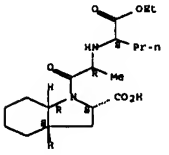
oxopropyl]octahydro-, [2R-[1[S*(R*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



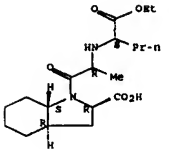
RN 145513-41-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



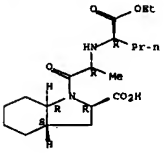
RN 145513-42-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(S*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



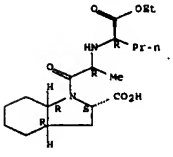
RN 145513-43-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(R*)],2α,3aα,7aβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 145513-44-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(S*)],2α,3aα,7aα]]- (9CI)
(CA INDEX NAME)

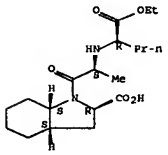
Absolute stereochemistry.



RN 145513-45-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-

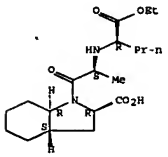
oxopropyl]octahydro-, [2R-[1[S*(R*)],2α,3aα,7aα]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



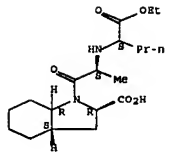
RN 145513-46-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(R*)],2α,3aα,7aβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



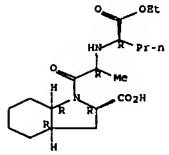
RN 145513-47-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(S*)],2α,3aα,7aβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



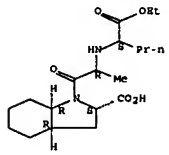
RN 145513-48-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2R)-2-[[(1R)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2R,3aR,7aR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 145513-49-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2α,3aα,7aα]]- (9CI)
(CA INDEX NAME)

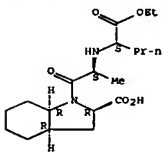
Absolute stereochemistry.



RN 145513-50-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-

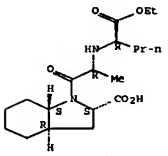
oxopropyl]octahydro-, [2R-[1[S*(S*)],2α,3aβ,7aβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



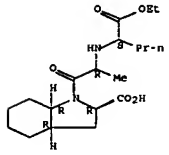
RN 145513-51-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(S*)],2α,3aα,7aβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



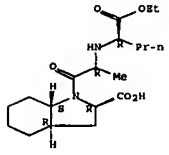
RN 145513-52-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(S*)],2α,3aβ,7aβ]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



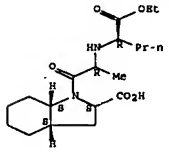
RN 145513-53-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(R*)],2α,3aβ,7aα]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 145513-54-8 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(S*)],2α,3aβ,7aβ]]- (9CI)
(CA INDEX NAME)

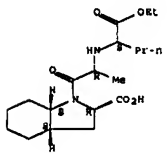
Absolute stereochemistry.



RN 145513-55-9 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2R)-2-[[(1S)-1-

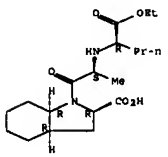
(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2R,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



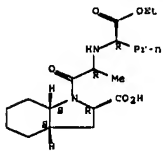
RN 145513-56-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[S*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



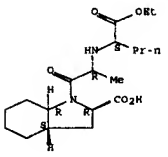
RN 145513-57-1 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(R*)],2α,3aα,7aα]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



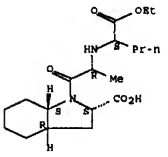
RN 145513-58-2 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2R-[1[R*(S*)],2α,3aα,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



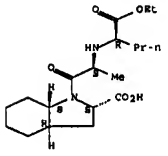
RN 145513-59-3 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[S*(R*)],2α,3aα,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



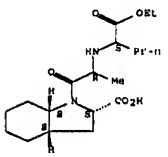
RN 145513-94-6 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R*(S*)],2α,3aα,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 130982-52-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 130982-52-4 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, monohydrochloride, [2S-[1[S*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L8 ANSWER 169 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1992:612157 CAPLUS Full-text
DN 117:212157
TI Preparation and formulation of [(mercaptoalkyl)carbamoyl]benzoates as analgesics and cardiovascular agents
IN Neustadt, Bernard R.
PA Schering Corp., USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9211235	A1	19920709	WO 1991-US9189	19911219

W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MW, PL, RO,

SD, SU, US
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG

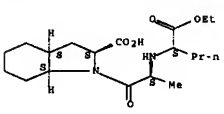
US 5232920	A	19930803	US 1990-633696	19901221
AU 9191046	A	19920722	AU 1991-91046	19911219
ZA 9110014	A	19920826	ZA 1991-10014	19911219
EP 563153	A1	19931006	EP 1992-901485	19911219
EP 563153	B1	19950315		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE

JP 05509331	T	19931222	JP 1992-501584	19911219
AT 119879	T	19950415	AT 1992-901485	19911219
ES 2072138	T3	19950701	ES 1992-901485	19911219
PRAI US 1990-633696	A2	19901221		
WO 1991-US9189	A	19911219		

OS MARPAT 117:212157
AB RSCH2CH[(CH2)mR1]NHCOR2 (R = H, CHO, alkanoyl, aroyl; R1 = (cyclo)alkyl, (hetero)aryl; R2 = ZCOR3, (substituted) heteroaryl; R3 = OH, (substituted) alkoxy, -amino; Z = (substituted) arylene; m = 1, 2) were prepared Thus, (S)-2-MeC6H4CH2CH(CH2SAc)CO2H was treated with (PhO)2P(O)N3 and Et3N in PhMe and the product condensed with PhCH2OH to give, after HBr/HOAc treatment, (R)-2-MeC6H4CH2CH(NH2)CH2SAc.HBr which was condensed with 3-(MeO2C)C6H4COCl to give, after saponification, (R)-2- MeC6H4CH2CH(CH2SH)NHCOC6H4(CO2H)-3. The latter gave 47 mmHg drop in blood pressure in exptl. hypertensive rats at 1 mg/kg orally.
IT 82834-16-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(compns. containing [(mercaptoalkyl)carbamoyl]benzoates and, as cardiovascular agents)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 170 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1992:114770 CAPLUS Full-text
DN 116:114770
TI Preparation of disulfide derivatives of mercaptoacylamino acids as cardiovascular agents
IN Haslanger, Martin F.; Neustadt, Bernard R.; Smith, Elizabeth M.
PA Schering Corp., USA
SO PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9117980	A1	19911128	WO 1991-US3251	19910515
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 9179572	A	19911210	AU 1991-79572	19910515
ZA 9103685	A	19920226	ZA 1991-3685	19910515
EP 528997	A1	19930303	EP 1991-911546	19910515
EP 528997	B1	19950201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05502038	T	19930415	JP 1991-510190	19910515
JP 06102648	B	19941214		
ES 2069893	T3	19950516	ES 1991-911546	19910515
PRAI US 1990-525370	A2	19900517		
WO 1991-US3251	A	19910515		

OS MARPAT 116:174770

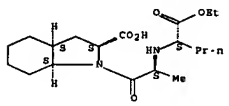
AB [SCH2CH(CH2R1)nCONHCHR2CHR4(CH2)t(CHR9)pCOR3]2, [SCH2CH(CH2R7)nCONHCHR2COR3 [R1 = alkyl, cycloalkyl, aryl, heteroaryl; R2 = H, alkyl, cycloalkyl, hydroxyalkyl, alkoxy, HS, alkylthio, aryl, heteroaryl, aralkyloxy, aralkylthio, R3 = R5O, R5R6N, R5, R6 = H, alkyl, hydroxyalkyl, etc., R5R6N = 5-7-membered ring; R4, R9 = (CH2)qR8, R8 = H, HO, alkoxy, HS, alkylthio, aryl, heteroaryl; R7 = (substituted) Ph; n = 1, 2; p, t = 0, 1; q = 0-2] useful in treatment of cardiovascular disorders and pain, are prepared To N-[3-mercapto-2(S)-(2-methylbenzyl)propionyl]-(S)- methionine Et ester (preparation given) in absolute EtOH was added iodine/EtOH to give 1,1'-[dithiobis[2(S)-(2-methylbenzyl)-1-oxo-3,1-propanediyl]]bis-(S)- methionine di-Et ester, which produced a drop in pressure in the DOCA salt model in the atrial natriuretic factor potentiation procedure. Pharmaceutical formulations containing the title compds. are given.

IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(pharmaceutical containing mercaptoacylamino acid disulfide and)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 171 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1992:120263 CAPLUS Full-text

DN 116:120263

TI A new radioimmunoassay for the determination of the angiotensin-converting enzyme inhibitor Perindopril and its active metabolite in plasma and urine: advantages of a lysine derivative as immunogen to improve the

assay specificity

AU Van den Berg, H.; Resplandy, G.; De Bie, A. T. H. J.; Floor, W.; Bertrand, M.; Arts, C. J. M.

CS CIVO Toxicol. Nutr. Inst., TNO, Zeist, 3700 AJ, Neth.

SO Journal of Pharmaceutical and Biomedical Analysis (1991), 9(7), 517-24
CODEN: JPBADA; ISSN: 0731-7085

DT Journal

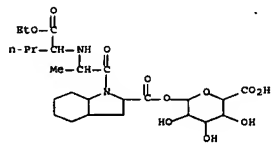
LA English

AB A new RIA was developed for the direct measurement of perindoprilat (PT), the active metabolite (diacid) of Perindopril (P), an angiotensin- converting enzyme (ACE) inhibitor. Antibodies were raised in rabbits against the lysine derivative of PT conjugated to bovine serum albumin. The p-hydroxyphenyl derivative of the lysine analog was used for preparation of the radioligand by iodination (125I). Cross-reactivities for the glucuronide metabolites of P and PT are low (0.25 and 3.5%, resp.). The theor. limit of detection is 0.2 nM, the sensitivity attainable with random samples is about 0.5 nM. Within- and between-assay variabilities observed were 4.2-6.7 and 2.8-5.9%, resp. (concentration range 2.1-41.7 nM). Serial dilution of plasma and urine samples showed excellent parallelism (r > 0.95). Recoveries of PT spiked to urine and plasma samples were 90-120%. The prodrug P can be measured in the same sample (plasma/urine) after chromatog. separation on a Dowex AG 1 × 2 anion-exchange column and quant. alkaline hydrolysis of the P-containing fraction. It is concluded that the specificity and sensitivity of this assay are amply sufficient for pharmacokinetic studies and in patient monitoring.

IT 120398-66-5
RL: ANST (Analytical study)
(cross-reactivity of, in RIA for determination of perindopril and its metabolite)

RN 120398-66-5 CAPLUS

CN β-D-Glucopyranuronic acid, 1-[1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate], [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

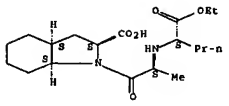


IT 82834-16-0, S-9490
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood plasma and urine, by RIA)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 172 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1991:74706 CAPLUS Full-text

DN 114:74706

TI Configuration and preferential solid-state conformations of perindoprilat (S-9780). Comparison with the crystal structures of other ACE inhibitors and conclusions related to structure-activity relationships

AU Pascard, Claudine; Guilhem, Jean; Vincent, Michel; Remond, Georges; Portevin, Bernard; Laubie, Michel

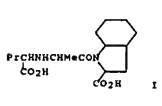
CS Inst. Chim. Subst. Nat., Gif-sur-Yvette, 91198, Fr.

SO Journal of Medicinal Chemistry (1991), 34(2), 663-9
CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

GI



I

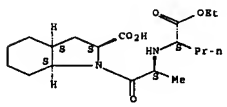
AB The conformational of perindoprilat (I), an antihypertensive drug, is studied in the solid state by X-ray anal. The resolution of its structure reveals important analogies between its observed conformation and that of several angiotensin-converting enzyme (ACE) inhibitors of the same family. This comparison points out a constant relative orientation of the functional groups, regardless of the mol. environment. This angular constancy appears not to be accidental and is a good argument for the spatial design of the ACE binding site. Although ACE is a carboxydipeptidase, the binding site may not contain two but one unique hydrophobic pocket receiving the C-terminal end of the inhibitors.

IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(saponification of)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 173 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1990:584168 CAPLUS Full-text

DN 113:184168

TI Interspecies comparison of the metabolic pathways of perindopril, a new angiotensin-converting enzyme (ACE) inhibitor

AU Grislain, L.; Mocquard, M. T.; Dabe, J. F.; Bertrand, M.; Luijten, W.; Marchand, B.; Resplandy, G.; Devissaguet, M.

CS Bio-Pharm. Serv., Orleans, 45000, Fr.

SO Xenobiotica (1990), 20(8), 787-800
CODEN: XENOBH; ISSN: 0049-8254

DT Journal

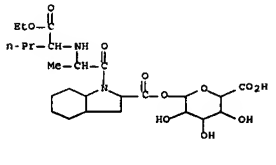
LA English

AB The metabolism of perindopril (non-thiol angiotensin-converting enzyme inhibitor) was studied in rat, dog and monkey after single oral and i.v. administration of 14C-perindorpil, and in man after a single oral dose. Six biotransformation in all species is the hydrolysis of the carboxylic Et ester side-chain, with the formation of perindoprilate, the active metabolite. A minor route of biotransformation led to the acyl glucuronides of perindopril and perindoprilate. Internal dehydration of perindopril and perindoprilate into cyclic lactam structures occurs. This route of metabolism is of minor importance except in humans.

IT 120398-66-5
RL: FORM (Formation, nonpreparative)
(formation of, as perindopril metabolite, in humans and laboratory animals)

RN 120398-66-5 CAPLUS

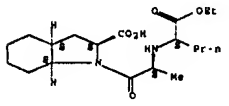
CN β-D-Glucopyranuronic acid, 1-[1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-1H-indole-2-carboxylate], [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)



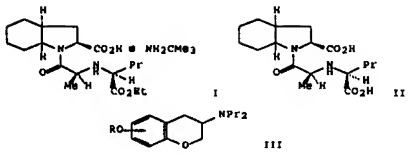
IT 82834-16-0
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(metabolism of, in humans and laboratory animals)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 174 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1990:118595 CAPLUS Full-text
DN 112:118595
TI Some syntheses of tritium biochemicals at high specific radioactivity: radiosyntheses of ACE inhibitors, 5-HT1A and dopamine receptors radioligands
AU Pichat, L.
CS CEA - CEN Saclay, Gif-sur-Yvette, 91191, Fr.
SO Synth. Appl. Isot. Labelled Cpd. 1988, Proc. Int. Symp. (1989), Meeting Date 1988, 21-6. Editor(s): Baillie, Thomas A.; Jones, John Richards. Publisher: Elsevier, Amsterdam, Neth.
CODEN: 56QXA6
DT Conference
LA English
GI



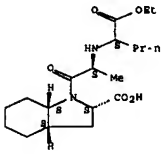
AB A lecture with 9 refs. Synthesis of tritium labeled biochems. I and II as potent inhibitors of angiotensin converting enzyme (ACE) and III (OR = 5-OMe, 8-OMe) as D2 receptors is described.
IT 125650-71-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as angiotensin converting enzyme inhibitors)

RN 125650-71-7 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, labeled with tritium, [2S-[1[R*(R*)],2α,3aβ,7aβ]]-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 125650-70-6
CMF C19 H32 N2 O5
CIL XH-13

Absolute stereochemistry.



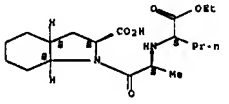
CM 2

CRN 75-64-9
CMF C4 H11 N

L8 ANSWER 175 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1989:586736 CAPLUS Full-text
DN 111:186736
TI Modeling, synthesis, and pharmacology of perindopril (S-9490), an inhibitor of angiotensin I-converting enzyme
AU Vincent, Michel; Schiavi, Pierre
CS Inst. Rech., SERVIER, Suresnes, 92150, Fr.
SO Colloque INSERM (1989), 181(Mec. Reconnaissance Mol.), 95-135
CODEN: CINMDE; ISSN: 0768-3154
DT Journal; General Review
LA French
AB A review with 4 refs.
IT 82834-16-0P, S-9490
RL: SPN (Synthetic preparation); PREP (Preparation)
(modeling and preparation and pharmacol. of, as angiotensin-converting

enzyme inhibitor)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

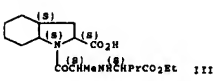
Absolute stereochemistry. Rotation (-).



L8 ANSWER 176 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1989:534746 CAPLUS Full-text
DN 111:134746
TI Preparation of N-[(alkoxycarbonyl)alkyl]-L-alanines as intermediates for carboxyalkyl dipeptides
IN Vincent, Michel; Baliarda, Jean; Marchand, Bernard; Remond, Georges
PA ADIR, Fr.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

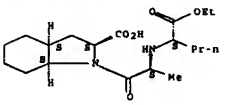
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 308340	A1	19890322	EP 1988-402338	19880916
EP 308340	B1	19910313		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620699	A1	19890324	FR 1987-12901	19870917
FR 2620699	B1	19900601		
CA 1340870	C	19990601	CA 1988-577077	19880907
DK 8805150	A	19890318	DK 1988-5150	19880915
DK 172005	B1	19970915		
AU 8822355	A	19890323	AU 1988-22355	19880916
AU 606992	B2	19910221		
JP 01110652	A	19890427	JP 1988-232124	19880916
JP 06099973	B	19941207		
ZA 8806930	A	19890530	ZA 1988-6930	19880916
US 4902817	A	19900220	US 1988-245353	19880916
AT 61566	T	19910315	AT 1988-402338	19880916
ES 2033451	T3	19930316	ES 1988-402338	19880916
PRAI FR 1987-12901	A	19870917		
EP 1988-402338	A	19880916		

OS CASREACT 111:134746; MARPAT 111:134746
GI



AB The title compds., (S,S)-HO2CCHMeNHCHR1CO2R2 (I; R1 = alkyl; R2 = H, alkyl), useful as intermediates for carboxyalkyl dipeptides R3CO-Q-COCHMeNHCHR2 (II; R3 = H, alkyl; Q = a residue of indoline, isoindoline, tetrahydroquinoline, perhydroindole, perhydroisoindole, perhydroisoquinoline, etc.), notably perindopril (III), an antihypertensive, are prepared via esterification of (S)-H2NCHR1CO2H (IV) with R2OH and reaction of the resulting (S)-H2NCHR1CO2R2 with pyruvic acid under catalytic hydrogenation conditions. (S)-H2NCHPrCO2Et (preparation given) was reacted with pyruvic acid under hydrogenation in the presence of Pd/C to give (S,S)-HO2CCHMeNHCHPrCO2Et.
IT 82834-16-0, Perindopril
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediate for, N-[(ethoxycarbonyl)butyl]alanine as)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



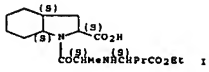
L8 ANSWER 177 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1989:515749 CAPLUS Full-text
DN 111:115749
TI Preparation of perindopril via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine
IN Vincent, Michel; Baliarda, Jean; Marchand, Bernard; Remond, Georges
PA ADIR, Fr.
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 308341	A1	19890322	EP 1988-402339	19880916
EP 308341	B1	19901212		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FR 2620709	A1	19890324	FR 1987-12896	19870917

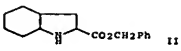
	FR 2620709	B1	19900907		
	CA 1336348	C	19950718	CA 1988-577078	19880907
	DK 8805151	A	19890318	DK 1988-5151	19880915
	DK 171470	B1	19961111		
	AU 8822362	A	19890323	AU 1988-22362	19880916
	AU 608363	B2	19910328		
	JP 01110696	A	19890427	JP 1988-232125	19880916
	JP 05043717	B	19930702		
	ZA 8806932	A	19890530	ZA 1988-6932	19880916
	US 4914214	A	19900403	US 1988-245446	19880916
	AT 59047	T	19901215	AT 1988-402339	19880916
	CA 1338015	C	19960130	CA 1991-616239	19911128
PRAI	FR 1987-12896	A	19870917		
	CA 1988-577078	A3	19880907		
	EP 1988-402339	A	19880916		

OS MARPAT 111:115749

GI



I



II

AB Preparation of perindopril via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine. The title compound (I), useful as an antihypertensive (no data), is prepared, e.g., via N-acylation of perhydroindole derivative II (preparation given) with (S,S)-HO2CCHMeNHCHPrCO2Et (III). II.p-MeC6H4SO3H (preparation given) was condensed with III in EtOAc containing Et3N, 1-hydroxybenzotriazole, and dicyclohexylcarbodiimide to give, after deprotection and treatment with Me3CNH2, I.Me3CNH2.

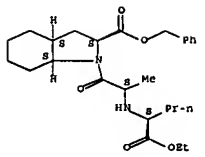
IT 122454-52-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)

RN 122454-52-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry.



IT 107133-36-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via acylation of perhydroindole derivative with N-[(ethoxycarbonyl)butyl]alanine)

RN 107133-36-8 CAPLUS

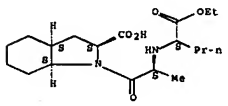
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0

CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9

CMF C4 H11 N

IT 82834-16-0P, Perindopril

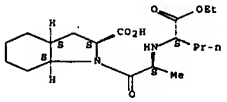
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, via acylation of perhydroindolecarboxylate with N-[(ethoxycarbonyl)butyl]alanine)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 178 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1989:515738 CAPLUS Full-text

DN 111:115738

TI Preparation of N-alkyl-α-amino acids and their derivatives as intermediates for carboxyalkyl dipeptides

IN Vincent, Michel; Baliarda, Jean; Marchand, Bernard; Remond, Georges

PA ADIR, Fr.

SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 309324	A1	19890329	EP 1988-402340	19880916
	EP 309324	B1	19910313		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	FR 2620700	A1	19890324	FR 1987-12902	19870917
	FR 2620700	B1	19900601		
	CA 1341380	C	20020806	CA 1988-577079	19880907
	DK 8805152	A	19890318	DK 1988-5152	19880915
	DK 173730	B1	20010806		
	AU 8822356	A	19890323	AU 1988-22356	19880916
	AU 607260	B2	19910228		
	JP 01110651	A	19890427	JP 1988-232122	19880916
	JP 07025723	B	19950322		
	ZA 8806933	A	19890530	ZA 1988-6933	19880916
	AT 61567	T	19910315	AT 1988-402340	19880916
	ES 2034324	T3	19930401	ES 1988-402340	19880916
	JP 07206792	A	19950808	JP 1994-241178	19941005
	JP 2524489	B2	19960814		
PRAI	FR 1987-12902	A	19870917		
	EP 1988-402340	A	19880916		

OS CASREACT 111:115738; MARPAT 111:115738

GI

V

AB (S,S)-HO2CCHMeNHCHR1CO2R2 (I; R1,R2 = lower alkyl), useful as intermediates for carboxyalkyl dipeptides R3CO-Q-COCHMeNHCHR1CO2R2 (II; R3 = H, alkyl; Q = residue of indoline, isoindoline, tetrahydroquinoline, tetrahydroisoquinoline, etc.), especially perindopril and its derivs., are prepared via (S)-H2NCHMeO2CH2Ph (III) with XCHR1CO2R2 (IV; X = halo), separation of (S,S) isomer from the resulting V, and deprotection by hydrogenolysis. III (preparation given) was reacted with IV (X = Br) in DMF containing Et3N to give V (R1 = Pr, R2 = Et), from which the (S,S) isomer was separated. This was hydrogenolyzed to give (S,S)-I (R1 = Pr, R2 = Et).

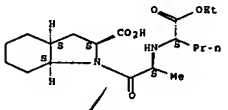
IT 82834-16-0P, Perindopril, derivs.

RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediates for, alkylamino acids as)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 179 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1989:477846 CAPLUS Full-text

DN 111:77846

TI Industrial preparation of (2S,3aS,7aS)-perhydroindole-2-carboxylic acid as intermediate for antihypertensive perindopril

IN Vincent, Michel; Baliarda, Jean; Marchand, Bernard; Remond, Georges

PA ADIR, Fr.

SO Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW

DT Patent

LA French

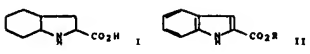
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 308339	A1	19890322	EP 1988-402337	19880916
	EP 308339	B1	19920506		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	FR 2620703	A1	19890324	FR 1987-12900	19870917
	FR 2620703	B1	19911004		
	DK 8805149	A	19890318	DK 1988-5149	19880915
	AU 8822361	A	19890323	AU 1988-22361	19880916

	AU 618752	B2	19920109		
	ZA 8806931	A	19890530	ZA 1988-6931	19880916
	US 4935525	A	19900619	US 1988-245352	19880916
	JP 02191251	A	19900727	JP 1988-232123	19880916
	AT 75735	T	19920515	AT 1988-402337	19880916
	ES 2033450	T3	19930316	ES 1988-402337	19880916
	US 4954640	A	19900904	US 1990-462797	19900110
PRAI	FR 1987-12900	A	19870917		
	EP 1988-402337	A	19880916		
	US 1988-245352	A3	19880916		

OS CASREACT 111:77846; MARPAT 111:77846

GI



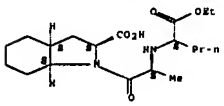
AB The title compound (I), useful as an intermediate for antihypertensive perindopril, was prepared from indolecarboxylic acid deriva. II (R = H, lower alkyl). Esterification of II (R = H) in EtOH containing H2SO4, reduction with Sn in EtOH containing HCl, saponification, and resolution gave (S)-indoline-2-carboxylic acid (III). Hydrogenation of III over Rh under H2 at 60° gave (2S,3aS,7aS)-octahydroindole-2-carboxylic acid.

IT 82834-16-0 107133-36-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(intermediate for, octahydroindolecarboxylic acid as)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



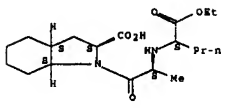
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

L8 ANSWER 180 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1989:204950 CAPLUS Full-text

DN 110:204950

TI Gas chromatography-mass spectrometry of perindopril and its active free metabolite, an angiotensin convertase inhibitor: choice of derivatives and ionization modes

AU Tsaconas, Christos; Devissaguet, Michele; Padieu, Prudent

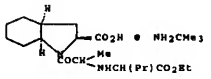
CS Cent. Spectrom. Masse, Fac. Med., Dijon, F-21033, Fr.

SO Journal of Chromatography (1989), 488(1), 249-65
CODEN: JOCRAM; ISSN: 0021-9673

DT Journal

LA English

GI



AB Perindopril (I), a perhydroindole compound and a novel class of angiotensin convertase inhibitor, after oral administration leads to an active metabolite by de-esterification of the Et ester. Routine biol. measurements are

currently done using a radioimmunol. assay, but a mass fragmento-graphic method was developed using plasma spiked with the drugs, which were then derivatized to the iso-Bu ester heptofluorobutyramide and assayed using ammonia neg. chemical ionization. Levels of 100 pg/mL were assayed. However, isobutanol derivatization provoked partial transesterification of the Et ester of the parent drug into the diisobutyl ester derivative, which corresponds to the active metabolite. A second method of derivatization to stable trimethylsilyl esters preserved the original Et ester of the parent drug. Despite the lower ionization yields, the mass fragmentog. method was sensitive and accurate enough to work satisfactorily at the 2 ng/mL level in spiked plasma, which is the level found currently in patients.

IT 107133-36-8, S-9490-3
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood plasma of humans by gas chromatog.-mass spectrometry, derivatization and ionization modes for)

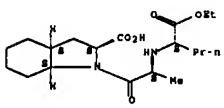
RN 107133-36-8 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (CA INDEX NAME)

CM 1

CRN 82834-16-0
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9
CMF C4 H11 N

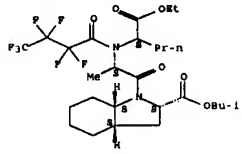
IT 120465-01-2P 120465-02-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 120465-01-2 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl](2,2,3,3,4,4,4-heptafluoro-1-oxobutyl)amino]-1-oxopropyl]octahydro-, 2-methylpropyl

ester, [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

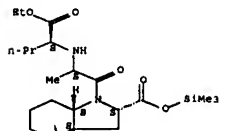
Absolute stereochemistry.



RN 120465-02-3 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, trimethylsilyl ester, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 181 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1988:631529 CAPLUS Full-text

DN 109:231529

TI Synthesis of S9490-3 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-(ethoxycarbonylbutyl)amino]-1-oxopropyl]-(2S,3aS,7aS)-perhydroindole-2-carboxylic acid tert-butylamine salt and S9780 [U-14C-cyclohexyl] 1-[(2S)2-[(1S)1-(carboxybutyl)amino]-1-oxopropyl]-2S,3aS,7aS)-perhydroindole-2-carboxylic acid and of [3,4-3H-butylamino]S9490-3 and [(3,4-3H-)butylamino]S9780

AU Pichat, L.; Tostain, J.; Gomis, J. M.; Coppo, M.; Moustier, A. M.; Vincent, M.; Remond, G.; Portevin, B.; Laubie, M.

CS CEN Saclay, Gif sur Yvette, 91191, Fr.

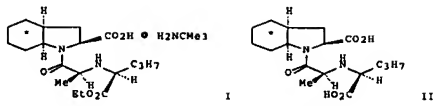
SO Journal of Labelled Compounds and Radiopharmaceuticals (1988), 25(5), 553-68
CODEN: JLCRD4; ISSN: 0362-4803

DT Journal

LA French

OS CASREACT 109:231529

GI



I II

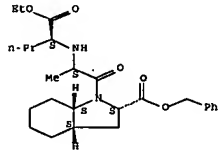
AB The title 14C-labeled compds. I (* signifies the uniform labeling of the cyclohexane ring with 14C) and II were prepared from aniline-U-14C in several steps. The title 3H-labeled compds. were also prepared The latter synthesis involved the tritiation of an allylglycine residue. The title compds. are potent inhibitors of angiotensin-converting enzyme.

IT 117770-57-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of)

RN 117770-57-7 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, phenylmethyl ester, labeled with carbon-14, [2S-[1[R*(R*)],2α,3aβ,7aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 117770-45-7P 117770-64-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

RN 117770-49-7 CAPLUS

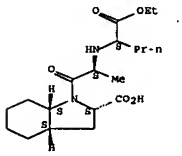
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, labeled with carbon-14, [2S-[1[R*(R*)],2α,3aα,7aβ]]-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 117770-48-6

CMF C19 H32 N2 O5
CIL XC-14

Absolute stereochemistry.

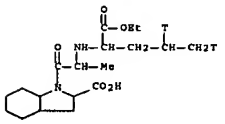


CM 2

CRN 75-64-9
CMF C4 H11 N

RN 117770-64-6 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl-3,4-t2]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)



L8 ANSWER 182 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1988:485650 CAPLUS Full-text
DN 109:85650
TI Biotransformation studies of di-acid angiotensin converting enzyme inhibitors
AU Drummer, O. H.; Kourtis, S.; Iakovidis, D.

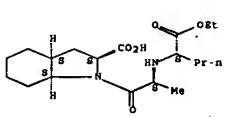
CS Austin Hosp., Univ. Melbourne, Heidelberg, Australia
SO Arzneimittel-Forschung (1988), 38(5), 647-50
CODEN: ARZNAD; ISSN: 0004-4172
DT Journal
LA English
GI For diagram(s), see printed CA Issue.
AB The biotransformation of di-acid angiotensin converting enzyme inhibitors perindopril (I), ramipril (II) and enalapril (III) to cyclized lactam metabolites was studied in the urine of rats using gas chromatog.-mass spectrometry. Chemical synthesis of the corresponding piperazinedione metabolites was achieved by reaction of I, II and III with Ac2O followed by hydrolysis of the ester group by Na in EtOH or by acid hydrolysis. Electron impact and chemical ionization mass spectra confirmed the structure of these potential novel metabolites. Selected ion monitoring of urinary exts. demonstrated small amts. (<5%) of these lactams for all 3 inhibitors. However, it was shown that the majority of these lactams were formed as a result of sample treatment rather than due to biotransformation.

IT 82834-16-0, Perindopril
RL: PROC (Process)
(biotransformation of, as diacid angiotensin converting enzyme inhibitor)

RN 82834-16-0 CAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 183 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1988:448448 CAPLUS Full-text
DN 109:48448
TI Neutral metalloendopeptidase inhibitors in the treatment of hypertension, compositions and kits containing the inhibitors, manufacture of the compositions, compounds of the compositions and their preparation
IN Haslanger, Martin F.; Sybertz, Edmund, Jr.; Neustadt, Bernard R.; Smith, Elizabeth M.
PA Schering Corp., USA
SO Eur. Pat. Appl., 167 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 254032	A2	19880127	EP 1987-108730	19870617
EP 254032	A3	19900905		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				

US 4749688	A	19880607	US 1986-876610	19860620
US 4801609	A	19890131	US 1987-32153	19870327
EP 566157	A1	19931020	EP 1993-107499	19870617
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI 8702720	A	19871221	FI 1987-2720	19870618
AU 8774458	A	19871224	AU 1987-74458	19870618
AU 602701	B2	19901025		
ZA 8704413	A	19880224	ZA 1987-4413	19870618
HU 44940	A2	19880530	HU 1987-2786	19870618
IL 82908	A	19910916	IL 1987-82908	19870618
DK 8703138	A	19871221	DK 1987-3138	19870619
NO 8702589	A	19871221	NO 1987-2589	19870619
JP 63039855	A	19880220	JP 1987-153219	19870619
JP 2542620	B2	19961009		
JP 08283153	A	19961029	JP 1995-246555	19870619
US 5061710	A	19911029	US 1987-133669	19871216
AU 9068517	A	19910718	AU 1990-68517	19901227
AU 636423	B2	19930429		
US 4801609	B1	19931109	US 1991-90002282	19910214
US 5262436	A	19931116	US 1991-741025	19910806
JP 08176100	A	19960709	JP 1995-246554	19950821
PRAI US 1986-876610	A	19860620		
US 1987-32153	A	19870327		
EP 1987-108730	A	19870617		
JP 1987-153219	A3	19870619		
US 1987-133669	A3	19871216		

OS MARPAT 109:48448

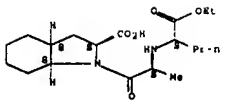
AB Neutral metalloendopeptidase (NMEP) inhibitor is used alone or combined with an atrial peptide or an angiotensin converting enzyme (ACE) inhibitor for preparation of pharmaceutical compns. for treating hypertension. The compns. are obtained by mixing a NMEP inhibitor, alone or combined with an atrial peptide or ACE inhibitor, with a pharmaceutically acceptable carrier. S-(4-Methylbenzyl)-L-cysteine, Me ester hydrochloride was prepared by adding thionyl chloride dropwise to N-tert-butyloxycarbonyl-S-(4- methylbenzyl)-L-cysteine in MeOH, heating the mixture under reflux for 90 min, cooling to room temperature, and concentrating in vacuo. Rats with induced hypertension were dosed s.c. with N-(N-[L-1-(2,2-dimethyl-1- oxopropoxy)methoxy]carbonyl)-2-phenylethyl)-L-phenylalanine]-β- alanine and 1-[(2S)-3-mercapto-2-methyl-1-oxypropyl]-L-proline in Me cellulose vehicle to give a 1-, 2-, 3-, and 4-h decrease in blood pressure of 14, 19, 19, and 15 mMHg vs. an increase of 14, 11, 11, and 8 with the NMEP inhibitor alone and a decrease of 11, 7, 1, and 1 mMHg with the ACE inhibitor alone.

IT 82834-16-0, Perindopril
RL: BIOL (Biological study)
(angiotensin converting enzyme inhibitor, antihypertensive containing neutral metalloendopeptidase inhibitor and)

RN 82834-16-0 CAPLUS

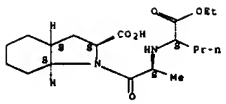
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 184 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1987:470497 CAPLUS Full-text
DN 107:70497
TI Angiotensin-converting enzyme inhibitors: measurement of relative inhibitory potency and serum drug levels by radioinhibitor binding displacement assay
AU Jackson, Bruce; Cubela, Rose; Johnston, Colin I.
CS Austin Hosp., Univ. Melbourne, Heidelberg, 3084, Australia
SO Journal of Cardiovascular Pharmacology (1987), 9(6), 699-704
CODEN: JCPCDT; ISSN: 0160-2446
DT Journal
LA English
AB Radioinhibitor binding displacement, a new method for the measurement of angiotensin-converting enzyme (ACE) competitive inhibitors, has been used to assess the relative potency of 9 synthetic ACE inhibitors. MK351A, a tyrosyl derivative of enalaprilic acid was iodinated with 125I and used as the radioligand. [125I]-MK351A bound to human serum ACE in a concentration-dependent manner. It was displaced in a concentration-dependent manner by all ACE inhibitors tested. Fifty percent displacement of bound [125I]MK351A (ID50) for each ACE inhibitor correlated well with inhibitor potency ID50, estimated using an ACE enzymic activity assay using Hip-His-Leu as substrate. The radioinhibitor binding displacement assay was used to measure serum concentration of enalaprilic acid (MK422) in human serum samples. Drug concentration estimated by radioinhibitor binding displacement assay correlated closely with the drug concentration measured by a specific radioimmunoassay. The radioinhibitor binding displacement technique using [125I]MK351A as the ligand for human serum ACE has general application to all competitive ACE inhibitors, allowing comparison of in vitro ACE inhibitor potencies and estimation of serum ACE inhibitor concns.
IT 82834-16-0, BB490
RL: BIOL (Biological study)
(angiotensin-converting enzyme of blood serum of humans inhibition by, assay for determining)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

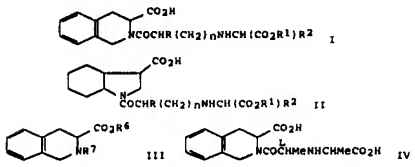


L8 ANSWER 185 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1982:616716 CAPLUS Full-text
DN 97:216716
TI Substituted imino diacids and pharmaceutical preparations containing them
IN Remond, Georges; Laubie, Michel; Vincent, Michel
PA Science Union et Cie., Societe Francaise de Recherche Medicale, Fr.
SO Eur. Pat. Appl., 38 pp.
CODEN: EPXXDW
DT Patent
LA French
FAN.CNT 2

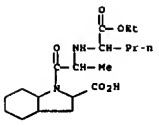
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 49658	A1	19820414	EP 1981-401501	19810929
	EP 49658	B1	19840613		
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	FR 2491469	A1	19820409	FR 1980-21095	19801002
	FR 2491469	B1	19830513		
	FR 2503155	A2	19821008	FR 1981-6916	19810407
	FR 2503155	B2	19830701		
	IL 63940	A	19850630	IL 1981-63940	19810925
	AT 7910	T	19840615	AT 1981-401501	19810929
	FI 8103034	A	19820403	FI 1981-3034	19810930
	FI 77230	B	19881031		
	FI 77230	C	19890210		
	DK 8104343	A	19820403	DK 1981-4343	19811001
	DK 157011	B	19891030		
	DK 157011	C	19900326		
	NO 8103339	A	19820405	NO 1981-3339	19811001
	NO 160780	B	19890220		
	NO 160780	C	19890531		
	AU 8175949	A	19820408	AU 1981-75949	19811001
	AU 542611	B2	19850228		
	HU 28405	A2	19831228	HU 1981-2838	19811001
	HU 185147	B	19841228		
	SU 1153827	A3	19850430	SU 1981-3344196	19811001
	CA 1341196	C	20010306	CA 1981-387093	19811001
	JP 57091974	A	19820608	JP 1981-157367	19811002
	JP 01032239	B	19890629		
	ZA 8106844	A	19820929	ZA 1981-6844	19811002
	ES 505999	A1	19830416	ES 1981-505999	19811002
	US 4508729	A	19850402	US 1981-308234	19811002
	US 4565819	A	19860121	US 1982-420005	19820920
	US 4616029	A	19861007	US 1984-659275	19841010
	US 4616031	A	19861007	US 1984-659276	19841010
	US 4644008	A	19870217	US 1984-659274	19841010
	US 4616030	A	19861007	US 1984-679320	19841206

PRAI	FR 1980-21095	A	19801002
	FR 1981-6916	A	19810407
	FR 1979-30046	A	19791207
	FR 1980-16875	A	19800731
	US 1980-212607	A2	19801203
	EP 1981-401501	A	19810929
	US 1981-308234	A1	19811002

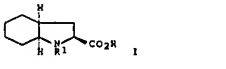
OS CASREACT 97:216716; MARPAT 97:216716
GI



AB Heterocyclic amino acid derivs., I and II [R = C1-4 alkyl; R1 = H, C1-4 alkyl; R2 = alkyl, mono- or dicycloalkylalkyl, phenylalkyl, (CH2)mXCHR3R4 [R3 = H, C1-4 alkyl, C3-6 cycloalkyl; R4 = H, C1-4 alkyl, C3-6 cycloalkyl, alkoxycarbonyl; X = S, NR5 (R5 = H, Ac, CO2CH2Ph), m = 1, 2]; n = 0, 1] were prepared Thus, (S)-phenylalanine was cyclized with H2CO to give (S)-isoquinoline (S)-III (R6 = R7 = H), which was esterified with MeOH/SOCl2 and then condensed with Boc-L-Ala-OH (Boc = Me3CO2C) by DCC/1-hydroxybenzotriazole to give (S)-III (R6 = Me, R7 = Boc-L-Ala). The latter was saponified and then Boc-deblocked by CF3CO2H to give (S)-III.CF3CO2H (R6 = H, R7 = H-L-Ala), which was treated with MeCOCO2H and then reduced by NaBH3CN to give isoquinoline (2S)-IV. I and II were useful as therapeutic agents due to their ability to inhibit enkephalinase, carboxypolypeptidase, kininase, and angiotensin-converting enzyme (ACE); e.g., the compds. can be used as antihypertensives since they inhibit ACE.
IT 82978-68-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 82978-68-5 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro- (9CI) (CA INDEX NAME)

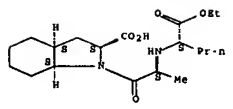


L8 ANSWER 186 OF 186 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1982:510360 CAPLUS Full-text
DN 97:110360
TI Stereoselective synthesis of a new perhydroindole derivative of chiral iminodiacid, a potent inhibitor of angiotensin converting enzyme
AU Vincent, M.; Remond, G.; Portevin, B.; Serkiz, B.; Laubie, M.
CS Inst. Rech. Servier, Suresnes, 92150, Fr.
SO Tetrahedron Letters (1982), 23(16), 1677-80
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
GI



AB The title enzyme inhibitor I (R = H, R1 = S,S-COCHMeNHCHPrCO2Et) (II) was prepared by coupling reaction of I (R = CMe3, R1 = H) (III) with (S,S)-HO2CCHMeN+H2CHPrCO2Et Cl- (IV). III was stereospecifically prepared from (S)-2-carboxyindoline in 5 steps; IV was stereoselectively prepared by reaction of PrCOCO2Et with (S)-H2NCHMeCO2CMe3 or by reaction of (S)-PrCH(CO2Et)N+H3 Cl- with MeCOCO2H. II showed 40% angiotensin converting enzyme inhibition after 24-30 h in dogs treated with 1 mg/kg p.o.
IT 82834-16-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and angiotensin converting enzyme inhibition by)
RN 82834-16-0 CAPLUS
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	981.63	1175.64
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-145.08	-145.08

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 11:29:22 ON 28 NOV 2007